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(54) Title: AMIDE DERIVATIVES AS SELECTIVE NEUROPEPTIDE Y RECEPTOR ANTAGONISTS

(57) Abstract

Amide derivatives having formula (I) or pharmaceutically acceptable salts thereof wherein R_1-R_5 are each individually selected from the group of substituents including hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkylalkenyl, alkylalkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocyle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, and cyano exhibit selective neuropeptide Y receptor antagonistic activity.

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AMIDE DERIVATIVES AS SELECTIVE NEUROPEPTIDE Y RECEPTOR ANTAGONISTS

BACKGROUND OF THE INVENTION

(1) Field of the Invention

This invention is a method for inhibiting the neuropeptide Y ("NPY") Y5 receptor using a class of amide derivatives. As antagonists of the Y5 receptor, the amide derivatives are useful in treating obese mammals, mammals with bulimia, for treating mammals with obesity related disorders including, but not limited to type II diabetes, insulin resistance hyperlipidemia, hypertension, polycystic ovarian disease, pulmonary disease, sleep apnea, and for treating mammals suffering from NPY Y5 receptor inhibition related disorders such as memory disorders, epilepsy, dyslipidemia, and depression.

(2) Description of the Art

NPY is a 36 amino acid peptide that is a member of a larger peptide family which includes peptide YY (PYY), and pancreatic peptide (PP). NPY is highly conserved in a variety of animal, reptile and fish species and is found mainly in the central and peripheral sympathetic neurons. Furthermore, NPY is the most prevalent peptide in the mammalian brain where it is found primarily in the limbic regions. NPY has been found to elicit a number of physiological responses including appetite stimulation, anxiolysis, hypertension, and regulation of coronary tone.

NPY is believed to stimulate food intake by activating a hypothalamic eating receptor. Hu et al., J. Bio. Chem., Vol. 271, No. 42 pp.26315-319 (1996) discloses the isolation and identification and the expression cloning of a novel Y-type receptor from rat hypothalamus which the authors designated Y5. According to Hu et al., the localization of Y5 mRNA in critical areas of the brain hypothalamus and other brain regions known to

regulate food intake together with an *in vitro* pharmacological profile consistent with the *in vivo* feeding data leads those skilled in the art to believe that the Y5 receptor is a primary mediator of NPY-induced feeding. A human homologue of the Y5 receptor has also been identified by Gerald et al., Nature, 382:168-171 (1996) which discloses the isolation, expression and analysis of an NPY Y5 receptor from the rat hypothalamus.

Antagonists of NPY receptors other than the Y5 receptors have been identified. For example, U.S. Patent No. 5,554,621 discloses NPY antagonists that act on the Y1, Y2, Y3 and other Y1-like or Y4-type receptors. The reported antagonists are dihydropyridine based substituents.

U.S. Patent No. 5,506,248 also discloses NPY receptor antagonists. The compositions disclosed each include sulphamadyl and amidino radicals. The disclosed compositions do not include amide moieties.

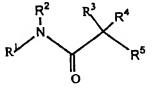
WO 96/16542 discloses genetically modified NPY receptors.

There is evidence that the Y5 receptor of NPY has a pharmacological feeding profile that is unique in comparison to other NPY receptors, namely, Y1, Y2, Y3 and Y4/PP1 because the Y5 receptor response correlates well with *in vivo* potencies of the standard peptides in the stimulation of feeding. Furthermore, antagonists of other NPY receptors such as Y1 do not necessarily exhibit an inhibitory response when assayed against Y5. In view of the knowledge that NPY plays an important role in eating and other disorders and in view of the knowledge that the Y5 receptor plays an important and unique role in the mechanism of such disorders, there is, therefore, a great need for antagonists of the NPY Y5 receptor. Furthermore, there is a need for antagonists of NPY that specifically target the Y5 receptor.

SUMMARY OF THE INVENTION

The present invention relates to methods for using amide derivatives that are NPY Y5 receptor antagonists to treat NPY mediated disorders including eating disorders such as bulimia and obesity. The present invention also includes novel amide derivatives. The amide derivative described immediately below, except for compounds 330-362 disclosed in Table 4 are novel, while all of the compounds described below, including compounds 137-188 disclosed in Table 4 are useful in the methods disclosed herein.

One object of this invention is a novel class of amide derivatives having the formula



(I)

except that compounds of this invention do not include compounds 330-362 identified in Table 4.

Another object of this invention is a method for treating obesity, obesity related disorders and eating disorders in mammals using a therapeutically effective amount of a composition heretofore unknown for its NPY Y5 inhibitory properties.

It is another object of this invention to provide a method for the effective treatment of diseases that include the NPY Y5 receptor in their mechanism.

It is still another object of this invention to provide a method for the treatment of obesity and bulimia in humans using a new class of amide derivatives.

Another object of this invention are novel amide derivatives of the compound of formula (I) that are useful as NPY Y5 receptor antagonists and therapeutic compositions containing the same.

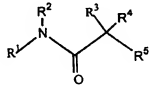
In one embodiment, this invention is a method for treating mammalian disorders mediated by the NPY Y5 receptor comprising the administration to a mammal of a therapeutically effective amount of at least one compound of formula (I) or pharmaceutically acceptable salts thereof wherein R_1-R_5 are each individually selected from the group of substituents including hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, and cyano.

In another embodiment, this invention is a method for treating mammalian disorders mediated by the NPY Y5 receptor comprising the administration to a mammal of a therapeutically effective amount of at least one compound having the general formula described above.

In yet another embodiment, this invention is a pharmaceutical dosage form comprising at least one amide derivative of a compound of formula (I) and at least one pharmaceutical additive.

DESCRIPTION OF THE CURRENT EMBODIMENT

The present invention relates to novel compositions that are NPY Y5 receptor antagonists and methods for using the compositions to treat NPY mediated disorders including eating disorders such as bulimia and obesity. Useful compositions of this invention are amide derivatives having the formula:



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In the composition, R^1-R^5 are each individually selected from the group of substituents including hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, and cyano. R^1 is preferably selected from: cyclohexyl; benzoyl; phenyl; phenyl substituted at least once with a lower alkyl that is in turn substituted at least once with a substituent selected from cycloalkyl, alkoxy, furan, oxo, phenyl, diisopropylamine, alkoxy, or mixtures thereof, lower alkyl, alkyl substituted at least once by oxo, phenyl, or by mixtures thereof, phenyl substituted alkene, carboxamide, carboalkoxy, methyl substituted carbophenoxy, phenyldiazo, halogen, nitro, trifluoroalkyl, amino, phenyl substituted amino, lower alkyl substituted amino, aminoacyl, sulfonylphenyl, hydroxy, alkoxy, fluoro substituted phenyl, oxazole, phenoxy, thioalkoxy, and mixtures thereof; hydroxy or alkoxy substituted naphthyl; 1H-indazole; fluorenone; fluorene; and phenyl.

R^2 is preferably hydrogen, or a lower alkyl.

R^3 is preferably hydrogen or lower alkyl, phenyl, and most preferably hydrogen.

R^4 is preferably hydrogen or lower alkyl, phenyl, and most preferably hydrogen or methyl.

R^5 is preferably selected from substituents including: pyrrolidine; pyrrolidine substituted at least once by amino, acylamino, trifluoroacylamino, hydroxyl, carboxyl, carbobenzyloxyamino, carbomethoxyamino, carbotertbutoxyamino, alkyl substituted carbotertbutoxyamino, pyridine, lower alkyl, alkene, carboxamide, hydroxymethyl, aminoalkyl, pyrolidinemethyl, alkoxy methyl, carboxylmethyl, hydroxymethyl substituted at least once by phenyl and mixtures thereof; morpholine; piperazine substituted at least once with benzyl, phenyl, halogen substituted phenyl, and mixtures thereof; unsubstituted piperidine; substituted piperidine; piperidine substituted at least once by 2-oxo-2,3-dihydrobenzimidaz-1-ol, unsubstituted lower alkyl, lower alkyl substituted at least once by aminoethylamino, iodide, =O, piperidine, hydroxymethyl substituted piperidine, acylamino, hydroxyl, phenyl, and mixtures thereof, cyano, halogen, cyanomethylphenyl, piperidine, pyrolidine, carboxyl, phenyl, phenyl substituted at least once by trifluoromethyl, lower alkyl, halogen, and mixtures thereof, 4-oxo-1-phenyl-1,3,8-triazaspiro[4.5dec-8-yl], hydroxyl, alkoxy, carboxyl amide having the formula $CONR^8R^9$ wherein R^8 and R^9 are each individually hydrogen or lower alkyl, or R^8 and R^9 are united with a nitrogen atom to form a piperidine substituent, amino alkyl having the formula $NR^{10}R^{11}$ where R^{10} and R^{11} are each individually selected from lower alkyl, cycloalkyl and phenyl, a ketone having the formula -COR^{12} where R^{12} is phenyl substituted by halogen or alkoxy or mixtures thereof; 3,6-dihydro-2H-pyridin-1-yl; halogen substituted phenyl substituted 3,6-dihydro-2H-pyridin-1-yl; 1,3,3-trimethyl-6-aza-bicyclo[3.2.1]octyl-6-yl; 2-aza-bicyclo[2.2.1]hept-6-yl; an amine

having the formula NR^6R^7 where R^6 and R^7 are the each individually selected from hydrogen, unsubstituted and substituted alkyl having from 1 to 10 carbon atoms, cycloalkyl, alkene, carboxy substituted alkene, lower alkyl substituted at least once by cyano, alkyne, cycloalkyl, hydroxyl, 2-hydroxyethoxy, pyridine, piperidine, pyrrolidine, piperazine, morpholine, methylpiperazine, 1-Methylpyrrol, phenyl, phenyl substituted at least once by alkoxy, halogen, carboxyl, phenoxy, hydroxy, nitro, iodine, and mixtures thereof, imidazole, 5-nitropyridylamino, furan, benzo[1,3]dioxol-5-yl, indole, alkoxy substituted indole, diethylamino, alkoxy, carboxy, trifluoromethyl, lower alkyl, hydroxymethyl, and mixtures thereof, benzyl, phenyl, benzo[1,2,5]thiadiazol, pyridine, 1,2,4-triazole, and 3-oxo-cyclohex-1-en.

The following definitions apply to certain terms used herein.

The term "halogen" refers to fluorine, bromine, chlorine, and iodine atoms.

The term "hydroxyl" refers to the group -OH.

The term "furan" refers to a five membered oxygen containing saturated or unsaturated heterocycle.

The term "oxo" refers to the group =O.

The term "thiol" and "mercapto" refers to the groups -SH, and $-S(O)_{0-2}$, respectively.

The term "lower alkyl" refers to a cyclic, branched, or straight chain alkyl group of one to ten carbon atoms. This term is further exemplified by such groups as methyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, i-butyl (or 2-methylpropyl), cyclopropylmethyl, i-amyl, n-amyl, hexyl and the like.

The term "substituted lower alkyl" refers to lower alkyl as just described including one or more substituents such as hydroxyl, thiol, alkylthiol, halogen, alkoxy, amino, amido, carboxyl, cycloalkyl, substituted cycloalkyl, heterocycle, cycloheteroalkyl, substituted

cycloheteroalkyl, acyl, carboxyl, aryl, substituted aryl, aryloxy, heteroaryl, substituted heteroaryl, arylalkyl, heteroarylalkyl, alkyl alkenyl, alkyl alkynyl, alkyl cycloalkyl, alkyl cycloheteroalkyl, and cyano. These groups may be attached to any carbon atom of the lower alkyl moiety.

The term "alkenyl" refers to a group -R'C=CR"R'" where R', R", R'" are each individually selected from hydrogen, halogen, lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl or the like.

The term "alkynyl" refers to a group -C≡C-R'; where R' is selected from hydrogen, halogen, lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl or the like.

The term "alkyl alkenyl" refers to a group -R-CR'=CR'"R'''', where R is lower alkyl, or substituted lower alkyl, R', R'", R'''' are each independently selected from hydrogen, halogen, lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, heteroaryl, or substituted heteroaryl.

The term "alkyl alkynyl" refers to a group -RC≡CR' where R is lower alkyl or substituted lower alkyl, R' is hydrogen, lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, heteroaryl, or substituted heteroaryl.

The term "alkoxy" refers to the group -OR, where R is lower alkyl, substituted lower alkyl, acyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroarylalkyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, or substituted cycloheteroalkyl.

The term "alkylthio" denotes the group -SR, $-S(O)_{n=1-2}-R$, where R is lower alkyl, substituted lower alkyl, aryl, substituted aryl, arylalkyl or substituted arylalkyl.

The term "acyl" refers to groups -C(O)R, where R is hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl and the like.

The term "aryloxy" refers to groups -OAr, where Ar is an aryl, substituted aryl, heteroaryl, or substituted heteroaryl group.

The term "amino" refers to the group NRR', where R and R' may independently be hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl, heteroaryl, cycloalkyl, substituted heteroaryl, or acyl.

The term "amido" refers to the group -C(O)NRR', where R and R' may independently be hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl.

The term "carboxyl" refers to the group -C(O)OR, where R may independently be hydrogen, lower alkyl, substituted lower alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl and the like.

The terms "aryl" and "Ar" refer to an aromatic carbocyclic group having at least one aromatic ring (e.g., phenyl or biphenyl) or multiple condensed rings in which at least one ring is aromatic, (e.g., 1,2,3,4-tetrahydronaphthyl, naphthyl, anthryl, or phenanthryl).

The term "substituted aryl" refers to aryl optionally substituted with one or more functional groups, e.g., halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

The term "heterocycle" refers to a saturated, unsaturated, or aromatic carbocyclic group having a single ring (e.g., morpholino, pyridyl or furyl) or multiple condensed rings (e.g., naphthpyridyl, quinoxalyl, quinolinyl, indolizinyl or benzo[b]thienyl) and having at least one hetero atom, such as N, O, or S, within the ring, which can optionally be unsubstituted or substituted with, e.g., halogen, lower alkyl, alkoxy, lower alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle,

heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

The term "heteroaryl" refers to a heterocycle in which at least one heterocyclic ring is aromatic.

The term "substituted heteroaryl" refers to a heterocycle optionally substituted with one or more substituents including halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

The term "arylalkyl" refers to the group -R-Ar where Ar is an aryl group and R is lower alkyl or substituted lower alkyl group. Aryl groups can optionally be unsubstituted or substituted with, e.g., halogen, lower alkyl, alkoxy, alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, thiol, sulfamido and the like.

The term "heteroalkyl" refers to the group -R-Het where Het is a heterocycle group and R is a lower alkyl group. Heteroalkyl groups can optionally be unsubstituted or substituted with e.g., halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

The term "heteroarylalkyl" refers to the group -R-HetAr where HetAr is a heteroaryl group and R is a lower alkyl or substituted lower alkyl. Heteroarylalkyl groups can optionally be unsubstituted or substituted with, e.g., halogen, lower alkyl, substituted lower alkyl, alkoxy, alkylthio, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

The term "cycloalkyl" refers to a divalent cyclic or polycyclic alkyl group containing 3 to 15 carbons. For polycyclic groups, these may be multiple condensed rings in which

one of the distal rings may be aromatic (*e.g.*, indanyl, tetrahydronaphthalene, etc. . . .).

The term "substituted cycloalkyl " refers to a cycloalkyl group comprising one or more substituents with, e.g., halogen, lower alkyl, substituted lower alkyl, alkoxy, alkylthio, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

The term "cycloheteroalkyl" refers to a cycloalkyl group wherein one or more of the ring carbon atoms is replaced with a heteroatom (e.g., N, O, S or P).

The term "substituted cycloheteroalkyl" refers to a cycloheteroalkyl group as herein defined which contains one or more substituents, such as halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

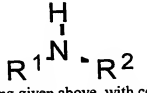
The term "alkyl cycloalkyl" refers to the group -R-cycloalkyl where cycloalkyl is a cycloalkyl group and R is a lower alkyl or substituted lower alkyl. Cycloalkyl groups can optionally be unsubstituted or substituted with e.g. halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, amino, amido, carboxyl, hydroxyl, aryl, aryloxy, heterocycle, heteroaryl, substituted heteroaryl, nitro, cyano, alkylthio, thiol, sulfamido and the like.

It is within the knowledge of one skilled in the art that stereoisomers of the compositions described herein as well as isomer and stereoisomers of components that comprise the compositions identified herein all fall within the scope of compositions that are useful in the therapeutic method of this invention.

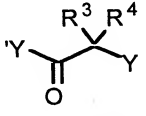
If the compound useful in the method of this invention contains a basic group, an acid addition salt may be prepared. Acid addition salts of the compounds are prepared in a

standard manner in a suitable solvent from the parent compound and an excess of acid, such as hydrochloric, hydrobromic, sulfuric, phosphoric, acetic, maleic, succinic, or methanesulfonic. If the final compound contains an acidic group, cationic salts may be prepared. Typically the parent compound is treated with an excess of an alkaline reagent, such as hydroxide, carbonate or alkoxide, containing the appropriate cation. Cations such as NA^+, K^+, Ca^{+2} and NH^{4+} are examples of cations present in pharmaceutically acceptable salts.

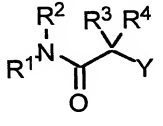
Compounds of formula (I) may be prepared by the following process. The process is characterized by the reaction of compounds of the general formula:



in which R^1 and R^2 have the meaning given above, with compounds of the general formula:

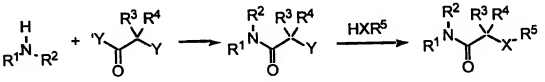


in which R^3 and R^4 have the meaning given above, and wherein 'Y represents halide, hydroxyl or O-acyl and wherein Y represents halide, preferably bromine. The reaction occurs in inert solvents and in the presence of base and/or auxiliaries, the later converted into compounds of the general formula:



in which R^1, R^2, R^3, R^4 and Y have the meaning given above. These compounds are reacted with amines of the general formula HR^5 in which R^5 have the meanings given above, in inert solvents, and, if appropriate in the presence of base and/or auxiliaries.

The process according to the invention can be illustrated by way of example by the following reaction scheme:



Suitable solvents for the process are customary organic solvents which do not change under the reaction conditions. These preferably include ethers such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether, or alcohols, for example methanol, ethanol, propanol, isopropanol, butanol, iso-butanol or tert-butanol, or hydrocarbons such as benzene, toluene, xylene, hexane, cyclohexane or petroleum fractions, or halogenated hydrocarbons such as dichloromethane, trichloromethane, tetrachloromethane, dichloroethylene, trichloroethylene or chlorobenzene, or ethyl acetate, triethylamine, pyridine, dimethylsulphoxide, dimethylformamide, hexamethylphosphoramide, acetonitrile, acetone or nitromethane. It is also possible to use mixtures of the solvents mentioned. Dimethylformamide and dimethylsulphoxide are preferred.

Bases which can be employed for the process are in general inorganic or organic bases. These preferably include alkali metal hydroxides, for example sodium hydroxide or potassium hydroxide, alkaline earth metal hydroxides, for example barium hydroxide, alkali metal carbonates such as sodium carbonate or potassium carbonate, alkaline earth metal carbonates such as calcium carbonate, or alkali metal or alkaline earth metal alkoxides such as sodium or potassium methoxide, sodium or potassium ethoxide or potassium tert-butoxide, or organic amines (trialkyl(C1-C6)-amines) such as triethylamine, or

heterocycles such as 1,4-diazabicyclo[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), pyridine, diaminopyridine, methylpiperidine or morpholine. It is also possible to employ as bases alkali metals such as sodium or their hydrides such as sodium hydride. Potassium carbonate is preferred.

The above mentioned bases can, if appropriate, also be employed as acid-binding auxiliaries. Suitable auxiliaries are also dehydrating reagents. These include, for example, carbodiimides such as diisopropylcarbodiimide, dicyclohexylcarbodiimide or N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride or carbonyl compounds such as carbonyldiimidazole or 1,2-oxazolium compounds such as 2-ethyl-5-phenyl-19 oxazolium-3-sulphonate or propanephosphonic anhydride or iso-butyl chloroformate or benzotriazolyloxy-tris-(dimethylamino)phosphonium hexafluorophosphate or diphenyl phosphoramidate or methane-sulphonyl chloride, if appropriate in the presence of bases such as triethylamine or N-ethylmorpholine or N-methylpiperidine or dicyclohexylcarbodiimide and N-hydroxysuccinimide.

The acid-binding agents and dehydrating reagents are in general employed in an amount from 0.5 to 3 mol, preferably from 1 to 1.5 mol, relative to 1 mol of the corresponding carboxylic acids. In general, the base is employed in an amount from 0.05 to 10 mol, preferably from 1 to 2 mol, relative to 1 mol of the compound of this invention.

The processes for manufacturing compounds according to the invention are in general carried out in a temperature of from about -30°C to about 110°C, preferably from about -10°C to about 50°C. The manufacturing processes are in general carried out at normal pressure. However, it is also possible to carry out the processes at elevated pressure or at reduced pressure (e.g. in a range from 0.5 to 5 bar).

The compounds described above (some of which are disclosed in Tables 1-2 below)

are useful for treating mammalian disorders such as eating disorders, obesity, hypertension, depression, brain or bodily disorders, and any other disorder mediated by NPY and the related Y5 receptor. It is preferred that the method of this invention is used to treat eating disorders such as obesity and bulimia. Specifically, the method of this invention can be used to inhibit the onset of obesity and to mediate the appetite in order to control and to reduce obese mammals such as humans. It is most preferred that the method of this invention is used to treat obesity and eating disorders in humans.

The compounds of the present invention are useful for treating disorders mediated by NPY via the Y5 receptor in mammals. For purposes of this disclosure, mammals includes humans, livestock, zoo animals, laboratory animals, experimental animals and pets. Livestock and related animals include, mammals such as cattle, horses, sheep, pigs, goats, camels, water buffaloes, donkeys, rabbits, fallow deer, reindeer; fur-bearing animals such as mink, chinchilla and raccoon; birds such as chickens, geese, turkeys and ducks. Laboratory animals and experimental animals include mice, rats, guinea pigs, golden hamsters, and pets include dogs, cats, rats, mice, guinea pigs, pigs, and the like.

The compounds of this invention may be administered to mammals both prophylactically and therapeutically by any administration protocol that is capable of supplying at least one compound of this invention to a Y5 receptor. Non-limiting examples of useful administration protocols include orally, parenterally, dermally, transdermally, rectally, nasally or by any other suitable pharmaceutical composition administration protocol that is within the knowledge of one skilled in the art.

The amide compositions of this invention will be administered in suitable pharmaceutical dosage forms. The pharmaceutical dosage form will depend largely upon the administration protocol used. The term pharmaceutical dosage form refers to items such as

tablets, capsules, liquids and powders, comprising Y5 receptor inhibitors of this invention alone or in the presence of one or more pharmaceutical excipients. The choice of additives such as excipients and adjuvants again will depend largely upon the chosen administration protocol. The compounds of this invention can also be incorporated into food products such as biscuits and cookies. In essence, the compositions can be used as a dietary supplement to reduce or inhibit appetite. Those skilled in the pharmaceutical arts will recognize a wide variety of formulations and vehicles for administering compositions of this invention.

The administration protocol will largely dictate the final form and composition of pharmaceutical dosage forms comprising the Y5 receptor antagonists of this invention. For example, internal administration of compounds of this invention is effected, orally, in the form of powders, tablets, capsules, pastes, drinks, granules, or solutions, suspensions and emulsions which can be administered orally, or boli, in medicated food, or in drinking water. Internal administration may also be accomplished using a timed release formulation including additives such as surfactant or starch coated capsules, or using a quick release formulation such as a freeze-dried fast dissolving tablet. Dermal administration is effected, for example, in the form of transdermal patches, spraying or pouring-on and spotting-on. Parenteral administration is effected, for example, in the form of injection (intramuscularly, subcutaneously, intravenously, intraperitoneally) or by implants.

Suitable pharmaceutical dosage forms incorporating the Y5 receptor antagonists of this invention include but are not limited to solutions such as solutions for injection, oral solutions, concentrates for oral administration after dilution, solutions for use on the skin or in body cavities, pour-on and spot-on formulations, gels; emulsions and suspension for oral or dermal administration and for injection; semi-solid preparations; formulations in which the active compound is incorporated in cream base or in an oil-in-water or water-in-oil

emulsion base; solid preparations such as powders, premixes or concentrates, granules, pellets, tablets, boli, capsules; aerosols and inhalants, and shaped articles containing active compound.

Pharmaceutical dosage forms that are solutions may be administered by injection intravenously, intramuscularly and subcutaneously. Solutions for injection are prepared by dissolving the active compound in a suitable solvent and, if appropriate, adding adjuvants such as solubilizers, acids, bases, buffer salts, antioxidants and preservatives. The solutions are sterile-filtered and drawn off.

Alternatively, solutions including compositions of this invention may be administered orally. Concentrates of compositions of this invention are preferably administered orally only after diluting the concentrate to the administration concentration. Oral solutions and concentrates are prepared as described above in the case of the solutions for injection. Solutions for use on the skin are applied dropwise, brushed on, rubbed in, splashed on or sprayed on. These solutions are prepared as described above in the case of solutions for injection.

Gels are applied to the skin, or introduced into body cavities. Gels are prepared by treating solutions which have been prepared as described in the case of the solutions for injection with such an amount of thickener that a clear substance of cream-like consistency is formed, or by any other means known to one skilled in the art.

Pour-on and spot-on formulations are poured onto, or splashed onto, limited areas of the skin, the active compound penetrating the skin and acting systemically. Pour-on and spot-on formulations are prepared by dissolving, suspending or emulsifying the active compound in suitable solvents or solvent mixtures which are tolerated by the skin. If appropriate, other adjuvants such as colorants, resorption accelerators, antioxidants, light

stabilizers, and tackifiers are added.

Emulsions can be administered orally, dermally or in the form of injections. Emulsions are either of the water-in-oil type or of the oil-in-water type. They are prepared by dissolving Y5 receptor antagonists either in the hydrophobic or in the hydrophilic phase and homogenizing the phase with a solvent of the opposite phase with the aid of suitable adjuvants such as emulsifiers, colorants, resorption accelerators, preservatives, antioxidants, light stabilizers, and viscosity-increasing substances.

Suspensions can be administered orally, dermally or in the form of injection. They are prepared by suspending the active compound in a liquid if appropriate with the addition of further adjuvants such as wetting agents, colorants, resorption accelerators, preservatives, antioxidants and light stabilizers.

The pharmaceutical compositions of this invention may include one or more additives in the form of pharmaceutically acceptable additives. Useful additives include solvents, solubilizers, preservatives, thickeners, wetting agents, colorants, resorption accelerators, antioxidants, light stabilizers, tackifiers, viscosity increasing substances, fillers, flavorings, lubricating agents, and any other pharmaceutical composition additive known to those skilled in the art.

The additive may be a solvent such as water, alcohols such as ethanol, butanol, benzyl alcohol, glycerol, propylene glycol, polyethylene glycols, N-methyl-pyrrolidone, alkanols, glycerol, aromatic alcohols such as benzyl alcohol, phenylethanol, phenoxyethanol, esters such as ethyl acetate, butyl acetate, benzyl benzoate, ethers such as alkylene glycol alkyl ethers such as dipropylene glycol mono-methyl ether, diethylene glycol mono-butyl ether, ketones such as acetone, methyl ethyl ketone, aromatic and/or aliphatic hydrocarbons, vegetable or synthetic oils, DMF, dimethylacetamide, N-methyl-

pyrrolidone, 2,2-dimethyl-4-oxy-methylene-1,3-dioxolane.

The following additives may be useful as solubilizers of the compositions of this invention: solvents which enhance solution of the active compound in the main solvent or which prevent its precipitation. Examples are polyvinylpyrrolidone, polyoxyethylated castor oil, polyoxyethylated sorbitan esters.

Useful preservatives are, for example, benzyl alcohol, trichlorobutanol, p-hydroxybenzoic esters, and n-butanol.

Useful thickeners include inorganic thickeners such as bentonite, colloidal silica, aluminum monostearate, organic thickeners such as cellulose derivatives, polyvinyl alcohols and their copolymers, acrylates and methacrylates.

Other liquids which may be useful in pharmaceutical dosage forms of this invention are, for example, homogeneous solvents, solvent mixtures, and wetting agents (dispersants) which are typically surfactants.

Useful colorants are all colorants which are non-toxic and which can be dissolved or suspended.

Useful resorption accelerators are DMSO, spreading oils such as isopropyl myristate, dipropylene glycol pelargonate, silicone oils, fatty acid esters, triglycerides, fatty alcohols.

Useful antioxidants are sulphites or metabisulphites such as potassium metabisulphite, ascorbic acid, butylhydroxytoluene, butylhydroxyanisole, tocopherol.

A useful light stabilizer is novantisolic acid.

Useful tackifiers include cellulose derivatives, starch derivatives, polyacrylates, natural polymers such as alginates, gelatin.

Useful emulsifiers include non-ionic surfactants such as polyoxyethylated castor oil,

polyoxyethylated sorbitan monooleate, sorbitan monostearate, glycerol monostearate, polyoxyethyl stearate, alkylphenol polyglycol ethers; ampholytic surfactants such as Di-Na N-lauryl- beta -iminodipropionate or lecithin; anionic surfactants, such as Na-lauryl sulphate, fatty alcohol ether sulphates, the monoethanolamine salt of mono/dialkylpolyglycol ether orthophosphoric esters; cationic surfactants such as cetyltrimethylammonium chloride.

Useful viscosity-increasing substances and substances which stabilize a therapeutic emulsion include carboxymethylcellulose, methylcellulose and other cellulose and starch derivatives, polyacrylates, alginates, gelatin, gum Arabic, polyvinylpyrrolidone, polyvinyl alcohol, copolymers of methyl vinyl ether and maleic anhydride, polyethylene glycols, waxes, colloidal silica or mixtures of the substances mentioned.

To prepare solid pharmaceutical dosage forms, the active compound is mixed with suitable additives, if appropriate with the addition of adjuvants, and the mixture is formulated as desired. Examples of physiologically acceptable solid inert additives include sodium chloride, carbonates such as calcium carbonate, hydrogen carbonates, aluminum oxides, silicas, clays, precipitated or colloidal silicon dioxide, and phosphates. Examples of solid organic additives include sugars, cellulose, foods such as dried milk, animal meals, cereal meals and coarse cereal meals and starches. Other suitable additives include lubricants and gliding agents such as magnesium stearate, stearic acid, talc, bentonites; disintegrants such as starch or crosslinked polyvinylpyrrolidone; binders such as, starch, gelatin or linear polyvinylpyrrolidone; and dry binders such as microcrystalline cellulose.

In the pharmaceutical dosage forms described herein, the active compounds can be present in the form of a mixture with at least one other Y5 receptor antagonist compound. Alternatively, or in addition, the pharmaceutical dosage forms of the invention can, in

addition to at least one Y5 receptor antagonist, include any pharmaceutical compound that is capable of treating any known malady or disorder where the administration of both together create no unacceptable adverse effects.

Methods for treating NPY mediated diseases and disorders comprises the administration of an effective quantity of the chosen compound or combinations thereof, preferably dispersed in a pharmaceutical dosage form. Ready-to-use pharmaceutical dosage forms of this invention contain the active compound in concentrations of from 10 ppm to 20 per cent by weight, and preferably of from 0.1 to 10 per cent by weight. Pharmaceutical dosage forms of this invention that are diluted prior to administration, preferably contain the active compound in concentrations of from 0.5 to 90 per cent by weight, and preferably of from 5 to 50 per cent by weight. In general, it has proved advantageous to administer amounts of approximately 0.01mg to approximately 100 mg of active compound per kg of body weight per day to achieve effective results.

The amount and frequency of administration of pharmaceutical dosage forms comprising Y5 receptor antagonists of this invention will be readily determined by one skilled in the art depending upon, among other factors, the route of administration, age and condition of the patient. These dosage units may be administered one to ten times daily for acute or chronic disease. No unacceptable toxicological effects are expected when compounds of the invention are administered in accordance with the present invention.

The pharmaceutical dosage forms comprising Y5 receptor antagonists of this invention are made following the conventional techniques of pharmacy involving milling, mixing, granulation, and compressing, when necessary, for tablet forms; or milling, mixing and filling for hard gelatin capsule forms. When a liquid additive is used, the preparation will be in the form of a syrup, elixir, emulsion or an aqueous or non-aqueous

suspension. Such a liquid formulation may be administered directly p.o. or filled into a soft gelatin capsule.

While the compositions described herein may be administered as described above, (*i.e.*, intramuscular, intravenous and subcutaneous etc...), it is preferred that the method of this invention is achieved by administering the compound described herein orally. When the oral administration route is chosen, a larger quantity of reactive agent will be required to produce the same effect as a smaller quantity given for example parenterally. In accordance with good clinical practice, it is preferred to administer the compound according to this method at a concentration level that would produce effective therapeutic results without causing any harmful side effects.

The compositions of this invention have non-therapeutic utility as well. The compositions of this invention are useful as analytical standards for Y5 receptor agonist or antagonist assays.

Compounds 1-329 identified in the Examples and in Tables 1 and 2 below are believed heretofore to be unknown. Known compounds that may be useful in the novel therapeutic method of this invention are compounds 330-3662 disclosed in Table 4 below.

EXAMPLES

The novel compounds useful in the therapeutic method of this invention are prepared by conventional methods of organic chemistry. Unless otherwise noted, reagents and solvents were obtained from commercial suppliers and were used without further purification.

The following solvent systems were used for analytical thin-layer chromatography (TLC): (A) ethyl acetate, (B) methylene chloride, (C) 9:1 dichloromethane:methanol, (D) 95:5 ethyl acetate:methanol, (E) 25:75 hexanes:ethyl acetate, (F) 7:3 hexanes:ethyl acetate, (G) 50:50 hexanes:ethyl acetate. TLC was performed on Merck Kieselgel 60 F_{254} silica gel plates (solvent systems A, C, D, and E); or, Baker Reversed Phase Octadecyl (C_{18}) plates (solvent system B). Detection was effected by exposure to UV light (254 nm) or by immersion in basic aqueous potassium permanganate solution. Chromatography was performed using Silica Gel 60 (#9385-5) from EM Science.

Melting points were recorded in open capillary tubes and are uncorrected.

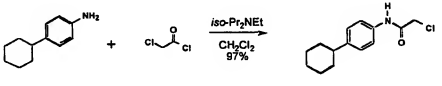
^1H NMR spectra were determined at 300 MHz using a General Electric GE-OMEGA 300 spectrometer. Chemical shifts are reported in parts per million (d) values relative to tetramethylsilane as internal standard. Spin multiplicities are reported using the following abbreviations: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Coupling constants are in Hertz.

Fast atom bombardment (FAB) mass spectra were recorded using a Kratos Concept 1 spectrometer; electron impact (EI) and chemical ionization (CI) mass spectra were recorded using a Hewlett-Packard MS Engine (HP5989A) spectrometer; liquid chromatography-mass spectra (LC-MS) were recorded using a Finningan MAT LCQ spectrometer.

Rainin high performance liquid chromatography (HPLC) systems with UV detectors at 254 nm were used under the following conditions: (N) C_{18} Reversed Phase Cartridge Column (Perkin Elmer/PE Xpress #0258-0164); 20:80 (0.1:99.9 trifluoroacetic acid-acetonitrile)-(0.1:2:97.9 trifluoroacetic acid-acetonitrile-water) to 95:5 (0.1:99.9 trifluoroacetic acid-acetonitrile)-(0.1:2:97.9 trifluoroacetic acid-acetonitrile-water) over 8 minutes, 95:5 (0.1:99.9 trifluoroacetic acid-acetonitrile)-(0.1:2:97.9 trifluoroacetic acid-acetonitrile-water) for 2 minutes; 3 mL/min. (O) Rainin Microsorb 80-225-C5 C_{18} Reversed Phase column with Microsorb 80-200-G5 C_{18} Reversed Phase guard column; 50:50 (0.1:99.9 trifluoroacetic acid-acetonitrile)-(0.1:2:97.9 trifluoroacetic acid-acetonitrile-water) to 100:0 (0.1:99.9 trifluoroacetic acid-acetonitrile)-(0.1:2:97.9 trifluoroacetic acid-acetonitrile-water) over 5 minutes, 0.1:99.9 trifluoroacetic acid-acetonitrile for 5 minutes; 1 mL/min.

EXAMPLE 1

Preparation of Intermediate - N-(4-Cyclohexyl-phenyl)-2-chloroacetamide:

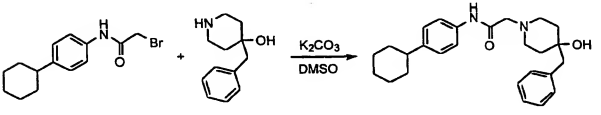


To 7.8 g (5.5 ml, 69.0 mmol) of chloroacetyl chloride in 200 ml of CH_2Cl_2 at 0°C, was added 12.0 g (69.0 mmol) of 4-cyclohexyaniline and 9.0 g (12.2 ml, 70.0 mmol). After warming to room temperature and stirring at room temperature for 1.5 hr, the reaction mixture was quenched with EtOAc. The organic layer was washed with 1N HCl, H_2O, and brine. The organic layer was separated and dried over $MgSO_4$, filtered and concentrated under reduced pressure to provide 16.8 g (97%) of the desired product. ^1H NMR (300 MHz, $CDCl_3$) d 8.20 (br s, 1H), 7.45 (d, 2H), 7.19 (d, 2H), 4.20 (s, 2H), 2.5 (br m, 1H),

1.95-1.70 (m, 4H), 1.45-1.2 (m, 4H). Using the same or analogous method, intermediates were prepared that were subsequently used according to the methods set forth in the Examples below to synthesize compounds of this invention.

EXAMPLE 2

Compound 1 : 2-(4-Benzyl-4-hydroxypiperidin-1-yl)-N-(4-cyclohexylphenyl)acetamide



A mixture of N-(4-cyclohexyl-phenyl)-2-bromoacetamide (29.6 mg, 0.10 mmol), 4-benzyl-4-hydroxypiperidine (19.1 mg, 0.10 mmol), and potassium carbonate (13.8 mg, 0.1 mmol) in dimethyl sulfoxide (1.0 mL) was stirred 1 hour. The mixture was filtered through a short pad of Celite in a pasteur pipet. TLC Rf 0.21 (silica gel, 50:50 hexane / ethyl acetate), 0.14 (reverse phase, 80:20 methanol / water); HPLC: 5.89 min (C18 Cartridge column (Perkin Elmer/PE Xpress #0258-0164) 20:80 Acetonitrile / water to 95:5 acetonitrile / water); LC-MS: 407 ($M + H^+$). The filtrate was tested directly in the in vitro biological assays.

The compounds of this invention that are set forth in Table 1, below, were prepared in analogy to the procedure of Example 2.

TABLE 1

Compound	NAME	TLC	MS	HPLC
2	N-(4-Cyclohexyl-phenyl)-2-dimethylamino-acetamide	ND	ND	ND
3	2-[4-(2-Chloro-phenyl)-piperazin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide	0.74 (A), 0.83 (B)	412 (M+H+, LC-MS)	11.45 (O)
4	2-[4-(4-Chloro-phenyl)-piperazin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide	0.55 (A), 0.83 (B)	412 (M+H+, LC-MS)	12.53 (O)
5	N-(4-Benzoyl-phenyl)-2-(2,2-dimethoxy-ethylamino)-acetamide	0.10 (A), 0.52 (B)	343 (M+H+, LC-MS)	5.03 (N)
6	N-(4-Benzoyl-phenyl)-2-morpholin-4-yl-acetamide	0.15 (A), 0.56 (B)	325 (M+H+, LC-MS)	3.88 (O)
7	N-(4-Benzoyl-phenyl)-2-diethylamino-acetamide	0.34 (A), 0.34 (B)	311 (M+H+, LC-MS)	4.42 (O)
8	N-(4-Benzoyl-phenyl)-2-[4-(2-chloro-phenyl)-piperazin-1-yl]-acetamide	0.47 (A), 0.83 (B)	434 (M+H+, LC-MS)	8.62 (O)
9	N-(4-Benzoyl-phenyl)-2-[4-(3-chloro-phenyl)-piperazin-1-yl]-acetamide	0.36 (A), 0.83 (B)	434 (M+H+, LC-MS)	8.71 (O)
10	N-(4-Benzoyl-phenyl)-2-[4-(4-chloro-phenyl)-piperazin-1-yl]-acetamide	0.31 (A), 0.55 (B)	434 (M+H+, LC-MS)	8.68 (O)
11	2-Benzylamino-N-(4-cyclohexyl-phenyl)-acetamide	ND	ND	ND
12	(4R,2S)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-hydroxy-pyrrolidine-2-carboxylic acid	0.31 (A), 0.41 (B)	347 (M+H+, LC-MS)	16.22 (O)
13	2-(4-Benzyl-piperazin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	0.30 (A), 0.34 (B)	392 (M+H+, LC-MS)	5.48 (N)
14	N-(4-Cyclohexyl-phenyl)-2-[(2-hydroxy-ethyl)-phenyl-amino]-acetamide	0.55 (A), 0.14 (B)	403 (LC-MS)	11.50 (O)
15	2-[4-(4-Chloro-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide	0.75 (A), 0.04 (B)	407 (LC-MS)	13.03 (O)
16	N-(4-Benzoyl-phenyl)-2-(4-benzyl-piperazin-1-yl)-acetamide	ND	ND	ND
17	N-(4-Benzoyl-phenyl)-2-[(2-hydroxy-ethyl)-phenyl-amino]-acetamide	ND	ND	ND
18	N-(4-Benzoyl-phenyl)-2-[4-(4-chloro-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-acetamide	0.41 (A), 0.15 (B)	431 (M+H+, LC-MS)	4.05 (O)
19	N-(4-Benzoyl-phenyl)-2-(4-benzyl-4-hydroxy-piperidin-1-yl)-acetamide	0.15 (A), 0.34 (B)	429 (M+H+, LC-MS)	3.16 (N)
20	(5S,2R)-1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-5-hydroxy-pyrrolidine-2-carboxylic acid	0.15 (A), 0.38 (B)	369 (M+H+, LC-MS)	3.81 (N)
21	N-(4-Benzoyl-phenyl)-2-(ethyl-pyridin-4-ylmethyl-amino)-acetamide	ND	ND	ND
22	N-(4-Benzoyl-phenyl)-2-(di-pyridin-2-yl-amino)-acetamide	0.34 (A), 0.45 (B)	409 (M+H+, LC-MS)	ND
23	N-(4-Cyclohexyl-phenyl)-2-[4-(3-piperidin-4-yl-propyl)-piperidin-1-yl]-acetamide	0.16 (A), 0.00 (B)	352 (LC-MS)	3.37 (N)
24	2-[1,4']Bipiperidinyl-1'-yl-N-(4-cyclohexyl-phenyl)-acetamide	0.70 (A), 0.10 (B)	391 (LC-MS)	2.79 (N)
25	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-piperidine-4-carboxylic acid	0.16 (A), 0.15 (B)	315 (LC-MS)	4.04 (N)
26	N-(4-Cyclohexyl-phenyl)-2-(4-hydroxy-4-phenyl-piperidin-1-yl)-acetamide	0.32 (A), 0.18 (B)	393 (M+H+, LC-MS)	4.12 (N)

Compound	NAME	TLC	MS	HPLC
28	N-(4-Cyclohexyl-phenyl)-2-[(piperidin-4-ylmethyl)-amino]-acetamide	0.16 (A), 0.00 (B)	384 (LC-MS)	2.52 (N)
29	N-(4-Cyclohexyl-phenyl)-2-(4-pyrrolidin-1-yl-piperidin-1-yl)-acetamide	0.16 (A), 0.10 (B)	384 (LC-MS)	2.67 (N)
30	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-methylamino-piperidine-4-carboxylic acid amide	0.16 (A), 0.30 (B)	373 (M+H+, LC-MS)	2.47 (N)
31	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-phenylamino-piperidine-4-carboxylic acid amide	0.16 (A), 0.25 (B)	435 (M+H+, LC-MS)	3.89 (N)
32	N-(4-Cyclohexyl-phenyl)-2-(4-dimethylamino-piperidin-1-yl)-acetamide	0.10 (A), 0.10 (B)	387 (LC-MS)	4.93 (N)
33	N-(4-Cyclohexyl-phenyl)-2-(4-methyl-piperidin-1-yl)-acetamide	0.20 (A), 0.06 (B)	370 (LC-MS)	6.32 (N)
34	N-(4-Cyclohexyl-phenyl)-2-(4,4-dimethyl-piperidin-1-yl)-acetamide	0.65 (A), 0.10 (B)	329 (M+H+, LC-MS)	4.15 (N)
35	4-Cyclohexylamino-1-[(4-cyclohexyl-phenylcarbamoyl)-methyl]-piperidine-4-carboxylic acid amide	0.15 (A), 0.15 (B)	441 (M+H+, LC-MS)	2.91 (N)
36	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-dimethylamino-piperidine-4-carboxylic acid amide	0.08 (A), 0.31 (B)	387 (M+H+, LC-MS)	2.47 (N)
37	N-(4-Benzoyl-phenyl)-2-[4-(3-piperidin-4-yl-propyl)-piperidin-1-yl]-acetamide	0.00 (A), 0.00 (B)	380 (LC-MS)	3.48 (N)
38	N-(4-Benzoyl-phenyl)-2-(4-benzyl-piperidin-1-yl)-acetamide	0.69 (A), 0.00 (B)	413 (M+H+, LC-MS)	5.04 (N)
39	N-(4-Benzoyl-phenyl)-2-[1,4']bipiperidinyl-1'-yl-acetamide	0.10 (A), 0.10 (B)	366 (LC-MS)	2.64 (N)
40	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-piperidine-4-carboxylic acid	0.28 (A)	367 (M+H+, LC-MS)	6.13 (N)
41	N-(4-Benzoyl-phenyl)-2-(4-hydroxy-4-phenyl-piperidin-1-yl)-acetamide	0.28 (A), 0.15 (B)	415 (M+H+, LC-MS)	4.14 (N)
42	N-(4-Benzoyl-phenyl)-2-(4-hydroxy-piperidin-1-yl)-acetamide	0.11 (A), 0.31 (B)	339 (M+H+, LC-MS)	2.94 (N)
43	N-(4-Benzoyl-phenyl)-2-[(piperidin-4-ylmethyl)-amino]-acetamide	0.11 (A)	ND	2.51 (N)
44	N-(4-Benzoyl-phenyl)-2-(4-cyano-4-phenyl-piperidin-1-yl)-acetamide	0.57 (A), 0.12 (B)	476 (LC-MS)	4.52 (N)
45	N-(4-Benzoyl-phenyl)-2-(4-pyrrolidin-1-yl-piperidin-1-yl)-acetamide	ND	352 (LC-MS)	2.77 (N)
46	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-methylamino-piperidine-4-carboxylic acid amide	0.28 (B)	395 (M+H+, LC-MS)	2.38 (N)
47	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-phenylamino-piperidine-4-carboxylic acid amide	0.10 (A), 0.23 (B)	457 (M+H+, LC-MS)	3.80 (N)
48	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-ethylamino-piperidine-4-carboxylic acid amide	0.10 (A), 0.23 (B)	409 (M+H+, LC-MS)	2.49 (N)
49	N-(4-Benzoyl-phenyl)-2-(4-dimethylamino-piperidin-1-yl)-acetamide		349 (LC-MS)	3.22 (N)
50	N-(4-Benzoyl-phenyl)-2-(4-methyl-piperidin-1-yl)-acetamide	0.57 (A), 0.07 (B)	337 (M+H+, LC-MS)	2.46 (N)
51	N-(4-Benzoyl-phenyl)-2-(4,4-dimethyl-piperidin-1-yl)-acetamide	0.62 (A), 0.08 (B)	351 (M+H+, LC-MS)	4.21 (N)

Compound	NAME	TLC	MS	HPLC
53	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-dimethylamino-piperidine-4-carboxylic acid amide	0.26 (B)	463 (LC-MS)	2.49 (N)
54	N-(4-Cyclohexyl-phenyl)-2-[4-(2-piperidin-4-yl-ethyl)-piperidin-1-yl]-acetamide	0.05 (A), 0.0.0 (B)	387 (LC-MS)	3.16 (N)
55	N-(4-Benzoyl-phenyl)-2-[4-(2-piperidin-4-yl-ethyl)-piperidin-1-yl]-acetamide	ND	349 (LC-MS)	1.82 (N)
56	2-[4-(Acetylamino-methyl)-4-phenyl-piperidin-1-yl]-N-(4-benzoyl-phenyl)-acetamide	0.10 (A), 0.42 (B)	470 (M+H+, LC-MS)	2.48 (N)
57	N-(4-Benzoyl-phenyl)-2-[4-(cyano-phenyl-methyl)-piperidin-1-yl]-acetamide	0.29 (A), 0.28 (B)	438 (M+H+, LC-MS)	3.37 (N)
58	N-(4-Benzoyl-phenyl)-2-(4-oxo-1-phenyl-1,3,8-triaza-spiro[4.5]dec-8-yl)-acetamide	0.07 (A), 0.28 (B)	469 (M+H+, LC-MS)	3.07 (N)
59	N-(4-Cyclohexyl-phenyl)-2-[4-(1-hydroxy-ethyl)-piperidin-1-yl]-acetamide	0.16 (A), 0.20 (B)	345 (M+H+, LC-MS)	3.13 (N)
60	N-(4-Benzoyl-phenyl)-2-[4-hydroxy-4-(3-phenyl-propyl)-piperidin-1-yl]-acetamide	0.12 (A), 0.25 (B)	457 (M+H+, LC-MS)	3.54 (N)
61	N-(4-Cyclohexyl-phenyl)-2-[4-hydroxy-4-(3-phenyl-propyl)-piperidin-1-yl]-acetamide	0.23 (A), 0.10 (B)	435 (M+H+, LC-MS)	4.88 (N)
62	N-(4-Cyclohexyl-phenyl)-2-[4-hydroxy-4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-acetamide	0.37 (A), 0.10 (B)	435 (LC-MS)	4.93 (N)
63	N-(4-Benzoyl-phenyl)-2-[4-hydroxy-4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-acetamide	0.12 (A), 0.33 (B)	483 (M+H+, LC-MS)	3.77 (N)
64	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-dimethylamino-piperidine-4-carboxylic acid amide	0.00 (A), 0.53 (B)	409 (M+H+, LC-MS)	0.90 (N)
65	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-dimethylamino-piperidine-4-carboxylic acid amide	0.11 (A), 0.29 (B)	387 (M+H+, LC-MS)	2.46 (N)
66	N-(4-Benzoyl-phenyl)-2-(4-phenyl-4-propoxy-piperidin-1-yl)-acetamide	0.54 (A), 0.10 (B)	457 (M+H+, LC-MS)	4.32 (N)
67	N-(4-Benzoyl-phenyl)-2-(4-{3-[1-(2-hydroxy-ethyl)-piperidin-4-yl]-propyl}-piperidin-1-yl)-acetamide	0.00 (A), 0.10 (B)	492 (M+H+, LC-MS)	1.96 (N)
68	N-(4-Cyclohexyl-phenyl)-2-(4-{3-[1-(2-hydroxy-ethyl)-piperidin-4-yl]-propyl}-piperidin-1-yl)-acetamide	0.11 (A), 0.00 (B)	470 (M+H+, LC-MS)	3.44 (N)
69	N-(4-Benzoyl-phenyl)-2-(4-phenyl-4-propionyl-piperidin-1-yl)-acetamide	0.46 (A), 0.28 (B)	455 (M+H+, LC-MS)	3.64 (N)
70	N-(4-Benzoyl-phenyl)-2-[4-(1-hydroxy-ethyl)-piperidin-1-yl]-acetamide	0.10 (A), 0.47 (B)	367 (M+H+, LC-MS)	1.74 (N)
71	N-(4-Benzoyl-phenyl)-2-(4-hydroxy-4-p-tolyl-piperidin-1-yl)-acetamide	0.20 (A), 0.37 (B)	429 (M+H+, LC-MS)	3.35 (N)
72	N-(4-Cyclohexyl-phenyl)-2-[4-phenyl-4-(piperidine-1-carbonyl)-piperidin-1-yl]-acetamide	0.31 (A), 0.08 (B)	488 (M+H+, LC-MS)	5.68 (N)
73	N-(4-Benzoyl-phenyl)-2-[4-phenyl-4-(piperidine-1-carbonyl)-piperidin-1-yl]-acetamide	0.20 (A), 0.24 (B)	510 (M+H+, LC-MS)	4.11 (N)
74	N-(4-Benzoyl-phenyl)-2-(4-butyryl-4-phenyl-piperidin-1-yl)-acetamide	0.47 (A), 0.32 (B)	469 (M+H+, LC-MS)	4.27 (N)

Compound	NAME	TLC	MS	HPLC
75	2-(4-Butyryl-4-phenyl-piperidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	0.10 (A), 0.10 (B)	448 (M+H+, LC-MS)	2.64 (N)
77	N-(4-Benzoyl-phenyl)-2-(2-pyridin-3-yl-pyrrolidin-1-yl)-acetamide	0.08 (A), 0.45 (B)	386 (M+H+, LC-MS)	1.52 (N)
78	N-(4-Benzoyl-phenyl)-2-(2S-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-acetamide	0.08 (A), 0.13 (B)	392 (M+H+, LC-MS)	1.59 (N)
79	N-(4-Cyclohexyl-phenyl)-2-(2S-pyrrolidin-1-ylmethyl-pyrrolidin-1-yl)-acetamide	0.28 (A), 0.15 (B)	370 (M+H+, LC-MS)	4.14 (N)
80	N-(4-Cyclohexyl-phenyl)-2-(3R-hydroxy-pyrrolidin-1-yl)-acetamide	0.11(A), 0.31 (B)	303 (M+H+, LC-MS)	2.94 (N)
81	N-(4-Benzoyl-phenyl)-2-(3R-hydroxy-pyrrolidin-1-yl)-acetamide	0.08 (A), 0.58 (B)	325 (M+H+, LC-MS)	1.52 (N)
82	N-(4-Benzoyl-phenyl)-2-[2R-(hydroxy-diphenyl-methyl)-pyrrolidin-1-yl]-acetamide	0.50 (A), 0.30 (B)	491 (M+H+, LC-MS)	4.16 (N)
83	N-(4-Cyclohexyl-phenyl)-2-[2R-(hydroxy-diphenyl-methyl)-pyrrolidin-1-yl]-acetamide	0.11 (A)	469 (M+H+, LC-MS)	2.51 (N)
84	N-(4-Cyclohexyl-phenyl)-2-(2S-hydroxymethyl-pyrrolidin-1-yl)-acetamide	0.57 (A), 0.12 (B)	317 (M+H+, LC-MS)	4.52 (N)
85	N-(4-Benzoyl-phenyl)-2-(2S-hydroxymethyl-pyrrolidin-1-yl)-acetamide	0.13 (A), 0.53 (B)	339 (M+H+, LC-MS)	1.79 (N)
86	2-(4-Acetyl-4-phenyl-piperidin-1-yl)-N-(4-benzoyl-phenyl)-acetamide	0.30 (A), 0.33 (B)	441 (M+H+, LC-MS)	3.47 (N)
87	2-(4-Acetyl-4-phenyl-piperidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	0.45 (A), 0.10 (B)	419 (M+H+, LC-MS)	4.82 (N)
88	2-[4-(4-Bromo-phenyl)-4-hydroxy-piperidin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide	0.22 (A), 0.10 (B)	472 (M+H+, LC-MS)	4.79 (N)
89	N-(4-Benzoyl-phenyl)-2-[4-(4-bromo-phenyl)-4-hydroxy-piperidin-1-yl]-acetamide	0.17 (A), 0.33 (B)	494 (M+H+, LC-MS)	3.58 (N)
90	(2R,4R)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-hydroxy-pyrrolidine-2-carboxylic acid	0.27 (A), 0.43 (B)	329 (LC-MS)	3.22 (N)
91	2-(2S-Aminomethyl-pyrrolidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	0.67 (A), 0.32 (B)	176 (LC-MS)	2.59 (N)
92	N-(4-Cyclohexyl-phenyl)-2-(3-hydroxy-pyrrolidin-1-yl)-acetamide	0.12 (A), 0.32 (B)	303 (M+H+, LC-MS)	3.02 (N)
93	N-(4-Cyclohexyl-phenyl)-2-(2S-methoxymethyl-pyrrolidin-1-yl)-acetamide	0.37 (A), 0.16 (B)	331 (M+H+, LC-MS)	3.91 (N)
94	N-(4-Cyclohexyl-phenyl)-2-((1S,5R)-1,3,3-trimethyl-6-aza-bicyclo[3.2.1]oct-6-yl)-acetamide	0.72 (A), 0.12 (B)	375 (LC-MS)	5.47 (N)
95	(2S)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid benzyl ester	0.27 (A), 0.33 (B)	518 (LC-MS)	4.80 (N)
96	(2S)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid methyl ester	0.27 (A), 0.42 (B)	234 (LC-MS)	4.82 (N)
97	2-(4-Bromo-piperidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	0.58 (A), 0.12 (B)	379 (M+, LC-MS)	4.12 (N)
98	(2S,4R)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-hydroxy-pyrrolidine-2-carboxylic acid	0.30 (A), 0.42 (B)	347 (M+H+, LC-MS)	6.24 (N)
99	(2S)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid	0.23 (A), 0.42 (B)	331 (M+H+, LC-MS)	6.63 (N)
100	2-(3-Amino-pyrrolidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	0.25 (A), 0.08 (B)	302 (M+H+, LC-MS)	4.83 (N)

Compound	NAME	TLC	MS	HPLC
101	(2R,4R)-1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-hydroxy-pyrrolidine-2-carboxylic acid	0.15 (A), 0.62 (B)	351 (LC-MS)	3.81 (N)
103	N-(4-Benzoyl-phenyl)-2-(3-hydroxy-pyrrolidin-1-yl)-acetamide	0.06 (A), 0.49 (B)	325 (M+H+, LC-MS)	1.52 (N)
104	N-(4-Benzoyl-phenyl)-2-(2S-methoxymethyl-pyrrolidin-1-yl)-acetamide	0.25 (A), 0.32 (B)	353 (M+H+, LC-MS)	2.36 (N)
105	N-(4-Benzoyl-phenyl)-2-((1S,5R)-1,3,3-trimethyl-6-aza-bicyclo[3.2.1]oct-6-yl)-acetamide	0.69 (A), 0.06 (B)	391 (M+H+, LC-MS)	3.83 (N)
106	(2S)-1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid benzyl ester	0.43 (A), 0.60 (B)	443 (M+H+, LC-MS)	3.22 (N)
107	(2S)-1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid methyl ester	ND	367 (M+H+, LC-MS)	3.22 (N)
108	N-(4-Benzoyl-phenyl)-2-(4-bromo-piperidin-1-yl)-acetamide	0.35 (A), 0.25 (B)	401 (M+, LC-MS)	2.61 (N)
109	(2S,4R)-1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-4-hydroxy-pyrrolidine-2-carboxylic acid	0.12 (A), 0.32 (B)	369 (M+H+, LC-MS)	3.82 (N)
110	(2S)-1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid	0.12 (A), 0.78 (B)	353 (M+H+, LC-MS)	4.67 (N)
111	N-(4-Benzoyl-phenyl)-2-(4-benzyl-4-hydroxy-piperidin-1-yl)-acetamide	0.12 (A), 0.29 (B)	429 (M+H+, LC-MS)	3.11 (N)
112	2-(3-Amino-pyrrolidin-1-yl)-N-(4-benzoyl-phenyl)-acetamide	0.10 (A), 0.06 (B)	324 (M+H+, LC-MS)	3.56 (N)
113	N-(4-Cyclohexyl-phenyl)-2-(2R-hydroxymethyl-pyrrolidin-1-yl)-acetamide	0.15 (A), 0.23 (B)	317 (M+H+, LC-MS)	3.30 (N)
114	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-2,2,5,5-tetramethyl-pyrrolidine-3-carboxylic acid amide	0.17 (A), 0.20 (B)	387 (M+H+, LC-MS)	3.84 (N)
115	(2S,3R,4R)-3-Carboxymethyl-1-[(4-cyclohexyl-phenylcarbamoyl)-methyl]-4-isopropenyl-pyrrolidine-2-carboxylic acid	0.24 (A), 0.36 (B)	429 (M+H+, LC-MS)	3.82 (N)
116	N-(4-Cyclohexyl-phenyl)-2-[4-(4-methoxy-benzoyl)-piperidin-1-yl]-acetamide	0.24 (A), 0.33 (B)	423 (LC-MS)	4.00 (N)
117	(2R)-1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid	0.05 (A), 0.37 (B)	331 (M+H+, LC-MS)	3.62 (N)
118	N-(4-Benzoyl-phenyl)-2-(2-hydroxymethyl-pyrrolidin-1-yl)-acetamide	0.13 (A), 0.47 (B)	339 (M+H+, LC-MS)	1.72 (N)
119	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-2,2,5,5-tetramethyl-pyrrolidine-3-carboxylic acid amide	0.15 (A), 0.43 (B)	408 (M+H+, LC-MS)	2.33 (N)
120	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-3-carboxymethyl-4-isopropenyl-pyrrolidine-2-carboxylic acid	0.15 (A), 0.24 (B)	451 (M+H+, LC-MS)	6.14 (N)
121	N-(4-Benzoyl-phenyl)-2-[4-(4-fluoro-benzoyl)-piperidin-1-yl]-acetamide	0.30 (A), 0.24 (B)	445 (M+H+, LC-MS)	3.54 (N)
122	N-(4-Benzoyl-phenyl)-2-[4-(4-methoxy-benzoyl)-piperidin-1-yl]-acetamide	0.15 (A), 0.60 (B)	515 (LC-MS)	2.69 (N)
123	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid amide	0.13 (A), 0.56 (B)	352 (M+H+, LC-MS)	1.58 (N)
124	1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid	0.13 (A), 0.64 (B)	353 (M+H+, LC-MS)	2.47 (N)
125	N-(4-Benzoyl-phenyl)-2-[2-(hydroxy-diphenyl-methyl)-pyrrolidin-1-yl]-acetamide	0.57 (A), 0.20 (B)	491 (M+H+, LC-MS)	4.20 (N)

Compound	NAME	TLC	MS	HPLC
126	N-(4-Cyclohexyl-phenyl)-2-[4-iodo-4-(2-iodo-ethyl)-piperidin-1-yl]-acetamide	0.63 (A), 0.14 (B)	561 (M+H+, LC-MS)	4.98 (N)
128	2-[4-(4-Chloro-benzoyl)-piperidin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide	0.40 (A), 0.10 (B)	439 (M+H+, LC-MS)	5.21 (N)
129	N-(4-Cyclohexyl-phenyl)-2-pyrrolidin-1-yl-acetamide	ND	ND	ND
130	N-(4-Cyclohexyl-phenyl)-2-(1H-[1,2,4]triazol-3-ylamino)-acetamide	0.18 (A), 0.45 (B)	373 (LC-MS)	3.21 (N)
131	2-(Benzhydryl-amino)-N-(4-cyclohexyl-phenyl)-acetamide	0.23 (A), 0.12 (B)	399 (M+H+, LC-MS)	5.24 (N)
132	N-(4-Cyclohexyl-phenyl)-2-[2-(1-methyl-1H-pyrrol-2-yl)-ethylamino]-acetamide	0.22 (A), 0.38 (B)	340 (M+H+, LC-MS)	7.79 (N)
133	N-(4-Benzoyl-phenyl)-2-[4-iodo-4-(2-iodo-ethyl)-piperidin-1-yl]-acetamide	0.47 (A), 0.34 (B)	603 (M+H+, LC-MS)	3.46 (N)
134	2-[4-[(2-Amino-ethylamino)-methyl]-piperidin-1-yl]-N-(4-benzoyl-phenyl)-acetamide	0.03 (A), 0.31 (B)	395 (M+H+, LC-MS)	1.13 (N)
135	N-(4-Benzoyl-phenyl)-2-[4-(4-chloro-benzoyl)-piperidin-1-yl]-acetamide	0.28 (A), 0.21 (B)	461 (M+H+, LC-MS)	3.93 (N)
136	N-(4-Benzoyl-phenyl)-2-pyrrolidin-1-yl-acetamide	ND	ND	ND
137	N-(4-Benzoyl-phenyl)-2-(1H-[1,2,4]triazol-3-ylamino)-acetamide	0.12 (A), 0.69 (B)	322 (M+H+, LC-MS)	1.93 (N)
138	2-(Benzhydryl-amino)-N-(4-benzoyl-phenyl)-acetamide	0.43 (A), 0.23 (B)	421 (M+H+, LC-MS)	4.00 (N)
139	N-(4-Benzoyl-phenyl)-2-[2-(1-methyl-1H-pyrrol-2-yl)-ethylamino]-acetamide	0.10 (A), 0.12 (B)	362 (M+H+, LC-MS)	5.31 (N)
140	N-(4-Cyclohexyl-phenyl)-2-decylamino-acetamide	0.14 (A), 0.10 (B)	ND	6.40 (N)
141	N-(4-Cyclohexyl-phenyl)-2-(3-phenyl-propylamino)-acetamide	0.14 (A), 0.10 (B)	351 (M+H+, LC-MS)	6.29 (N)
142	N-(4-Cyclohexyl-phenyl)-2-[2-(1H-imidazol-4-yl)-ethylamino]-acetamide	0.10 (B)	351 (LC-MS)	7.80 (N)
143	N-(4-Cyclohexyl-phenyl)-2-[2-(1H-indol-3-yl)-ethylamino]-acetamide	0.08 (A), 0.12 (B)	376 (M+H+, LC-MS)	6.05 (N)
144	N-(4-Cyclohexyl-phenyl)-2-[2-(5-methoxy-1H-indol-3-yl)-ethylamino]-acetamide	0.08 (A), 0.14 (B)	406 (M+H+, LC-MS)	6.69 (N)
145	N-(4-Cyclohexyl-phenyl)-2-[2-(4-methoxy-phenyl)-ethylamino]-acetamide	0.12 (A), 0.10 (B)	367 (M+H+, LC-MS)	ND
146	N-(4-Cyclohexyl-phenyl)-2-(2-piperazin-1-yl-ethylamino)-acetamide	0.06 (A)	345 (M+H+, LC-MS)	3.50 (N)
147	N-(4-Cyclohexyl-phenyl)-2-[2-(5-nitro-pyridin-2-ylamino)-ethylamino]-acetamide	0.06 (A)	398 (M+H+, LC-MS)	9.52 (N)
148	2-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-N-(4-cyclohexyl-phenyl)-acetamide	0.14 (A), 0.13 (B)	367 (M+H+, LC-MS)	5.53 (N)
149	N-(4-Cyclohexyl-phenyl)-2-(2-methoxy-benzylamino)-acetamide	0.14 (A), 0.11 (B)	353 (M+H+, LC-MS)	5.85 (N)
150	N-(4-Benzoyl-phenyl)-2-decylamino-acetamide	0.23 (A), 0.58 (B)	ND	4.45 (N)
151	N-(4-Benzoyl-phenyl)-2-(3-phenyl-propylamino)-acetamide	0.30 (A), 0.22 (B)	373 (M+H+, LC-MS)	7.20 (N)
152	N-(4-Benzoyl-phenyl)-2-[2-(1H-imidazol-4-yl)-ethylamino]-acetamide	0.23 (B)	349 (M+H+, LC-MS)	5.10 (N)

Compound	NAME	TLC	MS	HPLC
153	N-(4-Benzoyl-phenyl)-2-[2-(1H-indol-3-yl)-ethylamino]-acetamide	0.23 (A), 0.12 (B)	398 (M+H+, LC-MS)	6.81 (N)
155	N-(4-Benzoyl-phenyl)-2-[2-(4-methoxy-phenyl)-ethylamino]-acetamide	0.27 (A), 0.22 (B)	389 (M+H+, LC-MS)	6.93 (N)
156	N-(4-Benzoyl-phenyl)-2-(2-piperazin-1-yl-ethylamino)-acetamide	0.07 (A), 0.07 (B)	367 (M+H+, LC-MS)	2.07 (N)
157	N-(4-Benzoyl-phenyl)-2-[2-(5-nitro-pyridin-2-ylamino)-ethylamino]-acetamide	0.10 (A), 0.37 (B)	420 (M+H+, LC-MS)	6.32 (N)
158	2-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-N-(4-benzoyl-phenyl)-acetamide	0.17 (A), 0.31 (B)	389 (M+H+, LC-MS)	9.69 (N)
159	N-(4-Benzoyl-phenyl)-2-(2-methoxy-benzylamino)-acetamide	0.17 (A), 0.31 (B)	375 (M+H+, LC-MS)	5.70 (N)
160	N-(4-Cyclohexyl-phenyl)-2-[(furan-2-ylmethyl)-amino]-acetamide	0.37 (A), 0.22 (B)	313 (M+H+, LC-MS)	9.07 (N)
161	2-(2-Chloro-6-phenoxy-benzylamino)-N-(4-cyclohexyl-phenyl)-acetamide	0.66 (A), 0.06 (B)	448 (M+, LC-MS)	6.86 (N)
162	2-(Benzo[1,2,5]thiadiazol-4-ylamino)-N-(4-cyclohexyl-phenyl)-acetamide	0.74 (A), 0.11 (B)	367 (M+H+, LC-MS)	0.95 (N)
163	N-(4-Cyclohexyl-phenyl)-2-phenethylamino-acetamide	0.31 (A), 0.11 (B)	337 (M+H+, LC-MS)	9.57 (N)
164	N-(4-Cyclohexyl-phenyl)-2-(2,6-diiodo-4-nitro-phenylamino)-acetamide	0.22 (A), 0.06 (B)	337 (LC-MS)	4.97 (N)
165	4-[[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-amino]-3,5-diiodo-benzoic acid anion	0.56 (A), 0.11 (B)	603 (M+H+, LC-MS)	7.95 (N)
166	N-(4-Benzoyl-phenyl)-2-[(furan-2-ylmethyl)-amino]-acetamide	0.12 (A), 0.22 (B)	335 (M+H+, LC-MS)	6.02 (N)
167	N-(4-Benzoyl-phenyl)-2-(2-chloro-6-phenoxy-benzylamino)-acetamide	0.31 (A), 0.16 (B)	471 (M+H+, LC-MS)	7.90 (N)
168	2-(Benzo[1,2,5]thiadiazol-4-ylamino)-N-(4-benzoyl-phenyl)-acetamide	0.46 (A), 0.33 (B)	389 (M+H+, LC-MS)	0.93 (N)
169	N-(4-Benzoyl-phenyl)-2-phenethylamino-acetamide	0.11 (A), 0.11 (B)	359 (M+H+, LC-MS)	6.23 (N)
170	N-(4-Benzoyl-phenyl)-2-(2,6-diiodo-4-nitro-phenylamino)-acetamide	0.15 (A), 0.24 (B)	359 (LC-MS)	4.79 (N)
171	4-[[(4-Benzoyl-phenylcarbamoyl)-methyl]-amino]-3,5-diiodo-benzoic acid	0.45 (A), 0.24 (B)	627 (M+H+, LC-MS)	6.16 (N)
172	N-(4-Cyclohexyl-phenyl)-2-cyclopropylamino-acetamide	0.24 (A), 0.19 (B)	317 (LC-MS)	4.48 (N)
173	N-(4-Cyclohexyl-phenyl)-2-(2-hydroxy-1-hydroxymethyl-ethylamino)-acetamide	0.10 (A), 0.30 (B)	307 (M+H+, LC-MS)	2.91 (N)
174	N-(4-Cyclohexyl-phenyl)-2-(cyclopropylmethyl-amino)-acetamide	0.24 (A), 0.10 (B)	488 (LC-MS)	7.80 (N)
175	N-(4-Cyclohexyl-phenyl)-2-[3-(4-methyl-piperazin-1-yl)-propylamino]-acetamide	0.10 (A), 0.10 (B)	287 (LC-MS)	2.58 (N)
176	N-(4-Cyclohexyl-phenyl)-2-(2-hydroxy-ethylamino)-acetamide	0.10 (A), 0.23 (B)	277 (M+H+, LC-MS)	2.95 (N)
177	N-(4-Cyclohexyl-phenyl)-2-(2-hydroxy-1-hydroxymethyl-1-methyl-ethylamino)-acetamide	0.10 (A), 0.28 (B)	321 (M+H+, LC-MS)	3.07 (N)
178	N-(4-Cyclohexyl-phenyl)-2-(3-pyrrolidin-1-yl-propylamino)-acetamide	0.10 (A), 0.05 (B)	373 (M+H+, LC-MS)	2.77 (N)
179	N-(4-Cyclohexyl-phenyl)-2-(3-oxo-cyclohex-1-enylamino)-acetamide	0.22 (A), 0.21 (B)	327 (M+H+, LC-MS)	0.23 (N)

Compound	NAME	TLC	MS	HPLC
180	3-[[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-amino}-4,4,4-trifluoro-butyric acid	0.42 (A), 0.23 (B)	373 (M+H+, LC-MS)	3.69 (N)
182	N-(4-Benzoyl-phenyl)-2-cyclopropylamino-acetamide	0.14 (A), 0.19 (B)	344 (LC-MS)	4.61 (N)
183	N-(4-Benzoyl-phenyl)-2-(2-hydroxy-1-hydroxymethyl-ethylamino)-acetamide	0.58 (B)	329 (M+H+, LC-MS)	1.40 (N)
184	N-(4-Benzoyl-phenyl)-2-(cyclopropylmethyl-amino)-acetamide	0.13 (A), 0.21 (B)	309 (M+H+, LC-MS)	4.94 (N)
185	N-(4-Benzoyl-phenyl)-2-[3-(4-methyl-piperazin-1-yl)-propylamino]-acetamide	0.10 (B)	395 (M+H+, LC-MS)	1.23 (N)
186	N-(4-Benzoyl-phenyl)-2-(2-hydroxy-ethylamino)-acetamide	0.25 (B)	299 (M+H+, LC-MS)	1.41 (N)
187	N-(4-Benzoyl-phenyl)-2-(2-hydroxy-1-hydroxymethyl-1-methyl-ethylamino)-acetamide	0.15 (A), 0.56 (B)	343 (M+H+, LC-MS)	2.04 (N)
188	N-(4-Benzoyl-phenyl)-2-(3-pyrrolidin-1-yl-propylamino)-acetamide		366 (M+H+, LC-MS)	1.42 (N)
189	N-(4-Benzoyl-phenyl)-2-(3-oxo-cyclohex-1-enylamino)-acetamide	0.14 (A), 0.51 (B)	366 (LC-MS)	4.61 (N)
190	3-[[(4-Benzoyl-phenylcarbamoyl)-methyl]-amino}-4,4,4-trifluoro-butyric acid	0.25 (A), 0.41 (B)	395 (M+H+, LC-MS)	2.41 (N)
191	N-(4-Benzoyl-phenyl)-2-[2-(4-fluoro-phenyl)-1,1-dimethyl-ethylamino]-acetamide	0.60 (A), 0.41 (B)	405 (M+H+, LC-MS)	4.99 (N)
192	N-(4-Cyclohexyl-phenyl)-2-[2-(4-hydroxy-3-methoxy-phenyl)-ethylamino]-acetamide	0.20 (A), 0.42 (B)	383 (M+H+, LC-MS)	3.23 (N)
193	N-(4-Cyclohexyl-phenyl)-2-(3-methylamino-pyrrolidin-1-yl)-acetamide	0.05 (A), 0.24 (B)	598 (LC-MS)	2.64 (N)
194	{1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-carbamic acid tert-butyl ester	0.28 (A)	402 (M+H+, LC-MS)	4.67 (N)
195	{1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-carbamic acid tert-butyl ester	0.28 (A), 0.18 (B)	402 (M+H+, LC-MS)	4.52 (N)
196	N-(4-Cyclohexyl-phenyl)-2-(3-ethylamino-pyrrolidin-1-yl)-acetamide	0.13 (A)	346 (LC-MS)	2.68 (N)
197	N-{1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-2,2,2-trifluoro-acetamide	0.20 (A), 0.25 (B)	398 (M+H+, LC-MS)	4.14 (N)
198	N-(4-Cyclohexyl-phenyl)-2-(3-methylamino-pyrrolidin-1-yl)-acetamide	0.12 (B)	302 (LC-MS)	2.60 (N)
199	N-(4-Cyclohexyl-phenyl)-2-(3-ethylamino-pyrrolidin-1-yl)-acetamide	0.10 (A), 0.10 (B)	330 (M+H+, LC-MS)	2.67 (N)
200	N-(4-Cyclohexyl-phenyl)-2-(4-hydroxymethyl-piperidin-1-yl)-acetamide	0.10 (A), 0.26 (B)	331 (M+H+, LC-MS)	3.10 (N)
201	2-(Cyanomethyl-amino)-N-(4-cyclohexyl-phenyl)-acetamide	0.23 (A), 0.38 (B)	272 (M+H+, LC-MS)	4.11 (N)
202	N-(4-Benzoyl-phenyl)-2-[2-(4-hydroxy-3-methoxy-phenyl)-ethylamino]-acetamide	0.14 (A), 0.68 (B)	368 (LC-MS)	3.21 (N)
203	N-(4-Benzoyl-phenyl)-2-(3-methylamino-pyrrolidin-1-yl)-acetamide	0.05 (A), 0.22 (B)	338 (M+H+, LC-MS)	3.55 (N)
204	{1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-carbamic acid tert-butyl ester	0.14 (A), 0.63 (B)	424 (M+H+, LC-MS)	4.86 (N)
205	{1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-carbamic acid tert-butyl ester	0.14 (A), 0.37 (B)	424 (M+H+, LC-MS)	3.23 (N)
206	N-(4-Benzoyl-phenyl)-2-(3-ethylamino-pyrrolidin-1-yl)-acetamide	0.10 (B)	352 (M+H+, LC-MS)	1.28 (N)

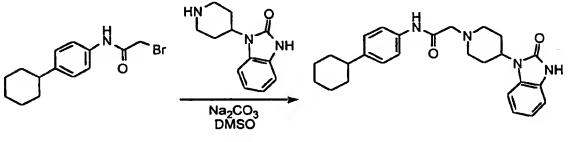
Compound	NAME	TLC	MS	HPLC
207	N-{1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-2,2,2-trifluoro-acetamide	0.10 (A), 0.48 (B)	420 (M+H+, LC-MS)	2.75 (N)
208	N-(4-Benzoyl-phenyl)-2-(3-methylamino-pyrrolidin-1-yl)-acetamide	0.05 (A), 0.10 (B)	338 (M+H+, LC-MS)	1.21 (N)
209	N-(4-Benzoyl-phenyl)-2-(3-ethylamino-pyrrolidin-1-yl)-acetamide	0.05 (A), 0.10 (B)	352 (M+H+, LC-MS)	1.37 (N)
210	N-(4-Benzoyl-phenyl)-2-(4-hydroxymethyl-piperidin-1-yl)-acetamide	0.10 (A), 0.49 (B)	353 (M+H+, LC-MS)	1.68 (N)
211	N-(4-Benzoyl-phenyl)-2-(cyanomethyl-amino)-acetamide	0.49 (A), 0.60 (B)	294 (M+H+, LC-MS)	1.91 (N)
212	4-({[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-amino}-methyl)-benzoic acid	0.28 (A), 0.39 (B)	367 (M+H+, LC-MS)	5.04 (N)
213	N-(4-Cyclohexyl-phenyl)-2-(1,1-dimethyl-prop-2-ynylamino)-acetamide	0.59 (A), 0.25 (B)	299 (M+H+, LC-MS)	3.67 (N)
214	2-(Cyclohexylmethyl-amino)-N-(4-cyclohexyl-phenyl)-acetamide	0.28 (A), 0.05 (B)	329 (M+H+, LC-MS)	4.91 (N)
215	{1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-methyl-carbamic acid tert-butyl ester	0.30 (A), 0.14 (B)	416 (M+H+, LC-MS)	5.39 (N)
216	N-(4-Cyclohexyl-phenyl)-2-(1-hydroxymethyl-butylamino)-acetamide	0.28 (A), 0.22 (B)	319 (M+H+, LC-MS)	7.64 (N)
217	N-(4-Cyclohexyl-phenyl)-2-(4-hydroxy-butylamino)-acetamide	0.07 (A), 0.20 (B)	305 (M+H+, LC-MS)	6.52 (N)
218	N-(4-Cyclohexyl-phenyl)-2-(3-morpholin-4-yl-propylamino)-acetamide	0.07 (A), 0.08 (B)	360 (M+H+, LC-MS)	7.02 (N)
219	N-(4-Cyclohexyl-phenyl)-2-(2-pyrrolidin-1-yl-ethylamino)-acetamide	0.07 (A)	520 (LC-MS)	7.03 (N)
220	2-[[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-amino}-pent-4-enoic acid	0.26 (A), 0.41 (B)	331 (M+H+, LC-MS)	5.02 (N)
221	Acetic acid 2-[(4-cyclohexyl-phenylcarbamoyl)-methyl]-2-aza-bicyclo[2.2.1]hept-6-yl ester	0.47 (A), 0.19 (B)	371 (M+H+, LC-MS)	3.87 (N)
222	4-({[(4-Benzoyl-phenylcarbamoyl)-methyl]-amino}-methyl)-benzoic acid	0.21 (A), 0.67 (B)	389 (M+H+, LC-MS)	3.44 (N)
223	N-(4-Benzoyl-phenyl)-2-(1,1-dimethyl-prop-2-ynylamino)-acetamide	0.53 (A), 0.50 (B)	321 (M+H+, LC-MS)	2.17 (N)
224	N-(4-Benzoyl-phenyl)-2-(cyclohexylmethyl-amino)-acetamide	0.27 (A), 0.17 (B)	351 (M+H+, LC-MS)	6.03 (N)
225	{1-[(4-Benzoyl-phenylcarbamoyl)-methyl]-pyrrolidin-3-yl}-methyl-carbamic acid tert-butyl ester	0.27 (A), 0.30 (B)	438 (M+H+, LC-MS)	3.84 (N)
226	N-(4-Benzoyl-phenyl)-2-(1-hydroxymethyl-butylamino)-acetamide	0.10 (A), 0.47 (B)	341 (M+H+, LC-MS)	4.95 (N)
227	N-(4-Benzoyl-phenyl)-2-(4-hydroxy-butylamino)-acetamide	0.05 (A), 0.30 (B)	327 (M+H+, LC-MS)	4.05 (N)
228	N-(4-Benzoyl-phenyl)-2-(3-morpholin-4-yl-propylamino)-acetamide	0.05 (A), 0.17 (B)	382 (M+H+, LC-MS)	4.30 (N)
229	N-(4-Benzoyl-phenyl)-2-(2-pyrrolidin-1-yl-ethylamino)-acetamide	0.63 (A), 0.05 (B)	352 (M+H+, LC-MS)	1.36 (N)
230	2-[[(4-Benzoyl-phenylcarbamoyl)-methyl]-amino}-pent-4-enoic acid	0.17 (A), 0.67 (B)	353 (M+H+, LC-MS)	3.43 (N)
231	Acetic acid 2-[(4-benzoyl-phenylcarbamoyl)-methyl]-2-aza-bicyclo[2.2.1]hept-6-yl ester	0.41 (A), 0.38 (B)	393 (M+H+, LC-MS)	2.43 (N)

Compound	NAME	TLC	MS	HPLC
233	4,4-Dicyano-3-[[(4-cyclohexyl-phenylcarbamoyl)-methyl]-amino}-but-3-enoic acid ethyl ester	0.20 (A), 0.40 (B)	387 (LC-MS)	5.00 (N)
234	N-(4-Cyclohexyl-phenyl)-2-(3-imidazol-1-yl-propylamino)-acetamide	0.05 (A), 0.15 (B)	341 (M+H+, LC-MS)	2.57 (N)
235	2-Allylamino-N-(4-cyclohexyl-phenyl)-acetamide	0.20 (A), 0.40 (B)	341 (M+H+, LC-MS)	7.32 (N)
236	N-(4-Cyclohexyl-phenyl)-2-(4-diethylamino-1-methyl-butylamino)-acetamide	0.05 (A), 0.05 (B)	374 (M+H+, LC-MS)	2.81 (N)
237	2-(2-Cyano-1-methyl-vinylamino)-N-(4-cyclohexyl-phenyl)-acetamide	0.22 (A), 0.40 (B)	374 (LC-MS)	5.00 (N)
238	3-[[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-amino}-but-2-enoic acid methyl ester	0.21 (A), 0.40 (B)	374 (M+H+, LC-MS)	5.00 (N)
239	2-Cyclohexylamino-N-(4-cyclohexyl-phenyl)-acetamide	0.39 (A), 0.07 (B)	315 (M+H+, LC-MS)	4.13 (N)
240	N-(4-Cyclohexyl-phenyl)-2-[2-(2-hydroxy-ethoxy)-ethylamino]-acetamide	0.10 (A), 0.28 (B)	321 (M+H+, LC-MS)	6.42 (N)
241	N-(4-Cyclohexyl-phenyl)-2-(2,2-dimethoxy-ethylamino)-acetamide	ND	ND	ND
242	N-(4-Benzoyl-phenyl)-2-cyclobutylamino-acetamide	0.12 (A), 0.24 (B)	309 (M+H+, LC-MS)	2.05 (N)
243	3-[[(4-Benzoyl-phenylcarbamoyl)-methyl]-amino}-4,4-dicyano-but-3-enoic acid ethyl ester	0.20 (A), 0.63 (B)	318 (LC-MS)	3.43 (N)
244	N-(4-Benzoyl-phenyl)-2-(3-imidazol-1-yl-propylamino)-acetamide	0.00 (A), 0.37 (B)	363 (M+H+, LC-MS)	1.18 (N)
245	2-Allylamino-N-(4-benzoyl-phenyl)-acetamide	0.17 (A), 0.13 (B)	295 (M+H+, LC-MS)	4.62 (N)
246	N-(4-Benzoyl-phenyl)-2-(4-diethylamino-1-methyl-butylamino)-acetamide	0.05 (A), 0.05 (B)	396 (M+H+, LC-MS)	1.50 (N)
247	N-(4-Benzoyl-phenyl)-2-(2-cyano-1-methyl-vinylamino)-acetamide	0.20 (A), 0.63 (B)	320 (M+H+, LC-MS)	3.43 (N)
248	3-[[(4-Benzoyl-phenylcarbamoyl)-methyl]-amino}-but-2-enoic acid methyl ester	0.20 (A), 0.63 (B)	352 (M+H+, LC-MS)	3.44 (N)
249	N-(4-Benzoyl-phenyl)-2-cyclohexylamino-acetamide	0.17 (A), 0.20 (B)	337 (M+H+, LC-MS)	5.30 (N)
250	N-(4-Benzoyl-phenyl)-2-[2-(2-hydroxy-ethoxy)-ethylamino]-acetamide	0.05 (A), 0.52 (B)	343 (M+H+, LC-MS)	1.47 (N)

EXAMPLE 3

This Example sets forth a second procedure that uses traditional techniques under the conditions described in Example 2 for synthesizing compounds of this invention.

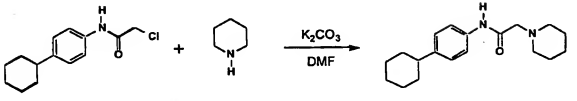
Compound 251: N-(4-Cyclohexyl-phenyl)-2-[4-(2-oxo-2,3-dihydrobenzoimidazol-1-yl)-piperidin-1-yl]-acetamide



A mixture of N-(4-cyclohexyl-phenyl)-2-bromoacetamide (50 mg, 0.17 mmol), 4-(2-keto-1-benzimidazolinyl)-piperidine (41 mg, 0.18 mmol), and potassium carbonate (34 mg, 0.25 mmol) in dimethylsulfoxide (2 mL) was stirred at room temperature for 2 hours. The mixture was diluted with water and extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with saturated aqueous sodium chloride solution, dried over $MgSO_4$, and concentrated to give a yellow oil. The crude oil was purified on reverse phase silica gel column using 100% acetonitrile to give N-(4-cyclohexyl-phenyl)-2-[4-(2-oxo-2,3-dihydrobenzoimidazol-1-yl)-piperidin-1-yl]-acetamide as a yellow solid (21 mg, 30%): mp 130-132°C. ^1H NMR (300 MHz, $CDCl_3$) d 9.28 (s, 1 H), 9.05 (s, 1 H), 7.53 (d, 2 H), 7.22 (d, 2 H), 7.11 (m, 4 H), 4.33 (m, 1 H), 3.22 (s, 2 H), 3.12 (d, 2 H), 2.40 - 2.60 (m, 5 H), 1.70 -1.90 (m, 7 H), 1.20 - 1.60 (m, 5 H). MS m/z 433 ($M+H^+$).

EXAMPLE 4

Compound 252: N-(4-Cyclohexyl-phenyl)-2-(piperidine)-acetamide



To 0.17 g of N-(4-cyclohexyl-phenyl)-2-chloroacetamide in 2.0 mL of DMF was added 0.11 g of K_2CO_3 and 0.1 mL of 1-piperidine. This mixture was stirred at rt for 2.5 hr. The reaction mixture was diluted with H_2O and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The product was redissolved in $CHCl_3$ and washed with H_2O and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to provided 0.129 g (62%) of the desired compound as a tan solid. mp=118-119°C; ^1H NMR (300 MHz, $CDCl_3$) d 9.18 (br s, 1H), 7.48 (d, J=8.5 Hz, 2H), 7.17 (d, J=8.5 Hz, 2H), 3.05 (s, 2H), 2.54-2.40 (m, 5H), 1.86-1.20 (m, 16H); MS (EI) m/e: 301 (M + H).

The compounds of this invention that were prepared in analogy to the procedure of Example 4 are set forth in Table 2, below.

TABLE 2

Compound	NAME	MP
253	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-propyl-phenyl)-acetamide	116-117
254	N-(4-Butyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	130-131
255	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-pentyl-phenyl)-acetamide	127-128
256	N-(4-Hexyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	128-129
257	N-(4-Isopropyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	133-134

Compound	NAME	MP
258	N-(4-Benzyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	182-3
259	N-(4'-Fluoro-biphenyl-4-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	228-9
260	4-[2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino}-benzoic acid isopropyl ester	166-7
261	(4-[2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino}-phenyl)-acetic acid ethyl ester	164-5
262	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-styryl-phenyl)-acetamide	234-5
263	N-(4-Benzoyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	215-6
264	4-[2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino}-benzoic acid P-tolyl ester; hydrochloride	197Z
265	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-[4-(oxo-phenyl-acetyl)-phenyl]-acetamide; hydrochloride	185Z
266	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(9-oxo-9H-fluoren-3-yl)-acetamide	175-6
267	N-(4-Oxazol-5-yl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrate	177-8
268	N-(3-Benzoyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	134-5
269	N-(4-Cyclohexyl-phenyl)-2-(4-oxo-1-phenyl-1,3,8-triaza-spiro[4.5]dec-8-yl)-acetamide	117-118
270	N-(4-Cyclohexyl-phenyl)-N-methyl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	250-253
271	N-Biphenyl-4-yl-2-piperidin-1-yl-acetamide	102-103
272	N-(4-Cyclohexyl-phenyl)-2-(4-phenyl-piperazin-1-yl)-acetamide	195-196
273	2-(Benzhydryl-amino)-N-(4-cyclohexyl-phenyl)-acetamide	132-133
274	N-(4-Cyclohexyl-phenyl)-2-[4-(3-phenyl-ureido)-piperidin-1-yl]-acetamide	222-223
275	N-Biphenyl-4-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	180-181
276	N-(4-Cyclohexyl-phenyl)-2-[3-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-propylamino]-acetamide	
277	N-Biphenyl-4-yl-2-[3-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-propylamino]-acetamide	
278	N-(4-Cyclohexyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-propionamide	148-150
279	N-(4-#tertl-Butyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-propionamide	144-148
280	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-phenethyl-acetamide; hydrochloride	181-2
281	N-(2-Diisopropylamino-ethyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	195-6
282	N-Cyclohexylmethyl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	196-7
283	N-(3-Isopropoxy-propyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	237-8
284	N-(2-Methoxy-ethyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	77-8
285	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(tetrahydro-furan-2-ylmethyl)-acetamide	179-80

Compound	NAME	MP
288	N-Cyclopentyl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; compound with oxalic acid	217-8
289	N-(3-Isopropoxy-propyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	67-8
290	2-(3-Acetylamino-pyrrolidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide	105-110
291	2-(Benzyl-ethyl-amino)-N-(4-cyclohexyl-phenyl)-acetamide	
292	N-(4-Cyclohexyl-phenyl)-2-[4-(4-fluoro-benzoyl)-piperidin-1-yl]-acetamide; hydrochloride	258
293	2-(3-Acetylamino-pyrrolidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide; compound with oxalic acid	122
294	N-(4-Cyclohexyl-phenyl)-2-(4-phenyl-4-propoxy-piperidin-1-yl)-acetamide; hydrochloride	
295	2-(4-Cyano-4-phenyl-piperidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide; hydrochloride	
296	N-(4-Cyclohexyl-phenyl)-2-[2-(hydroxy-diphenyl-methyl)-pyrrolidin-1-yl]-acetamide; compound with oxalic acid	
297	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-pyrrolidine-2-carboxylic acid amide; hydrochloride	
298	N-(4-Cyclohexyl-phenyl)-2-(4-hydroxy-4-p-tolyl-piperidin-1-yl)-acetamide; hydrochloride	
299	2-[4-(2-Chloro-phenyl)-piperazin-1-yl]-N-(4-cyclohexy-phenyl-acetamide; compound with oxalic acid	
300	2-[4-(Cyano-phenyl-methyl)-piperidin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide; hydrochloride	150
301	2-[4-(Acetylamino-methyl)-4-phenyl-piperidin-1-yl]-N-(4-cyclohexyl-phenyl)-acetamide; compound with oxalic acid	146
302	1-[(4-Cyclohexyl-phenylcarbamoyl)-methyl]-4-ethylamino-piperidine-4-carboxylic acid amide; compound with oxalic acid	184
303	N-(4-Cyclohexyl-phenyl)-2-(4-phenyl-4-propionyl-piperidin-1-yl)-acetamide; hydrochloride	252
304	2-(3-Acetylamino-pyrrolidin-1-yl)-N-(4-benzoyl-phenyl)-acetamide; compound with oxalic acid	100
305	1-[1-(2-Azocan-1-yl-2-oxo-ethyl)-piperidin-4-yl]-1,3-dihydro-benzoimidazol-2-one; hydrochloride	158
306	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(9-oxo-9H-fluoren-2-yl)-acetamide; hydrochloride	204
307	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(9-oxo-9H-fluoren-1-yl)-acetamide; hydrochloride	204
308	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(9-oxo-9H-fluoren-4-yl)-acetamide	205
309	1-[1-(2-Azepan-1-yl-2-oxo-ethyl)-piperidin-4-yl]-1,3-dihydro-benzoimidazol-2-one	166
310	N-Dibenzofuran-2-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	186
311	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(9-oxo-9H-fluoren-3-yl)-acetamide; hydrochloride	258
312	N-Biphenyl-4-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-2-phenyl-acetamide	207-210
313	N-(4-Cyclohexyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-2-phenyl-acetamide	217-210
314	2-(4-Benzyl-4-hydroxy-piperidin-1-yl)-N-(4-cyclohexyl-phenyl)-acetamide; hydrochloride	
315	2-(4-Benzyl-4-hydroxy-piperidin-1-yl)-N-biphenyl-4-yl-acetamide; hydrochloride	
316	N-Biphenyl-4-yl-2-[2-(4-hydroxy-3-methoxy-phenyl)-ethylamino]-acetamide; hydrochloride	

Compound	NAME	MP
317	N-Biphenyl-4-yl-2-(4-phenyl-4-propionyl-piperidin-1-yl)-acetamide; hydrochloride	
319	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-phenylamino-phenyl)-acetamide; hydrochloride	
322	N-Benzhydryl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	
323	N-Biphenyl-3-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	
324	N-Biphenyl-2-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	
325	N-(9H-Fluoren-2-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	
326	N-Bicyclo[2.2.1]hept-2-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	
327	N-(4'-Fluoro-biphenyl-4-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	289
328	N-(4-Methoxy-biphenyl-3-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; hydrochloride	
329	N-Biphenyl-4-yl-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-propionamide; hydrochloride	

EXAMPLE 5

The compounds prepared in Examples 2-4 as well as the prior art compounds set forth in Table 4, below, were tested for NPY Y5 receptor binding affinity according to one or more of the protocols set forth below.

A. Human NPY1 Receptor Binding Assay

This is a modification of Gordon et al., (J. Neurochem. 55:506-513, 1990). SK-N-MC cells (ATCC, Rockville, MD) were plated in 24-well plates. Once confluent, cells were rinsed with Dulbecco's phosphate buffered saline (DPBS). Cells were then preincubated in binding buffer containing serum-free DMEM, 25 mM HEPES (pH 7.3), 0.5% bovine serum albumin (BSA), 0.1% bacitracin and 0.1 mM phenylmethylsulfonylfluoride for 30 minutes at room temperature. Drug dilution and [125I]PYY (~50 pM: NEN-DuPont) were added to the wells, and the cells were incubated for an additional 3 hours at room temperature, followed by rinsing with ice-cold DPBS. Nonspecific binding was defined with 1 μM

NPY.. After lysing the cells with 1% Triton X-100, the amount of radioactivity in the lysates was quantitated with a gamma counter. IC50 values, which correspond to 50% inhibition of specific binding, were determined with non-linear regression analysis. The results of compounds tested according to this protocol are reported in Table 3.

B. Human Y2 and Y4/PP1 Receptor Binding Assays

Binding assays were performed on GF/C Millipore 96-well plates pretreated with 0.02% polyethylenimine. The binding buffer for rat Y2 binding is Krebs-Ringer bicarbonate (pH 7.4) containing 0.01% BSA and 0.005% bacitracin. Samples consist of membrane protein, 25 pM [125I]PYY and drug dilution. Nonspecific binding is defined by 1 μM NPY. The binding buffer for human Y4/PP1 binding consists of 137 mM NaCl, 5.4 mM KCl, 0.44 mM KH2PO4, 1.26 mM CaCl2, 0.81 mM MgSO4, 20 mM HEPES, 1 mM dithiothreitol, 0.1% bacitracin, 100 mg/l streptomycin sulfate, 1 mg/l aprotinin, 10 mg/ml soybean trypsin inhibitor and 0.3% BSA, pH 7.4. Samples consist of membrane protein, 50 pM human [125I]human PP (hPP: NEN DuPont, Boston, MA) and drug dilution. 1 μM hPP is used to define nonspecific binding.

After a 2 hour incubation at room temperature with constant mixing, the samples are aspirated on a vacuum manifold, and rinsed with ice-cold binding buffer. The amount of radioactivity in each well is quantitated with either gamma counting or liquid scintillation. IC50 values, which correspond to 50% inhibition of specific binding, are determined with non-linear regression analysis. The results of compounds tested according to this protocol are reported in Table 3.

C. Human and Rat NPY5 Receptor Binding Assays

Binding assays are performed on GF/C Millipore 96-well plates pretreated with 0.02% polyethylenimine. The binding buffer is 25 mM Tris, 120 mM NaCl, 5 mM KCl, 1.2 mM KH2PO4, 2.5 mM CaCl2, 1.2 mM MgSO4, 0.1% BSA and 0.5 mg/ml bacitracin, pH 7.4. Samples consist of membrane protein, 75-100 pM [125I]PYY (porcine, NEN-DuPont) and drug dilution. Nonspecific binding is defined by 1 μM PYY. After a 2 hour incubation at room temperature with constant mixing, the samples are aspirated on a vacuum manifold, and rinsed with ice-cold binding buffer. The amount of radioactivity in each well is quantitated with either gamma counting or liquid scintillation. IC50 values, which correspond to 50% inhibition of specific binding, are determined with non-linear regression analysis. The results of compounds tested according to this protocol are reported in Table 3.

D. Rat NYP5 Cyclase Assay (In Vitro Functional Assay)

Cells stably expressing the rat NPY5 receptor are resuspended in serum-free DMEM containing 10 mM HEPES (pH 7.4) and 1 mM isobutylmethylxanthine (IBMX). 1 mM forskolin and drug dilution are then added to the cells. After a 20 minute incubation of the samples at 37°C, the assay is stopped by placing the samples in boiling water for 3 minutes. The cAMP produced in each sample is quantitated with a radioimmunoassay kit (NEN DuPont). Data are expressed as a percentage of forskolin-stimulated adenylate cyclase. The results of compounds tested according to this protocol are reported in Table 3.

TABLE 3

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
	IC50 (μM)	IC50 (μM)	IC50 (μM)	IC50 (μM)	IC50 (μM)	%FSAC (10μM)
1	ND	>5	ND	0.15	ND	ND
2	ND	>5	ND	0.78	ND	ND
3	ND	>5	ND	0.19	ND	ND
4	ND	>5	ND	0.53	ND	ND
5	ND	ND	ND	0.3	0.3	ND
6	ND	>5	ND	0.8	ND	ND
7	ND	>5	ND	1.6	ND	ND
8	ND	>5	ND	0.96	ND	ND
9	ND	>5	ND	0.64	ND	ND
10	ND	>5	ND	2.9	ND	ND
11	ND	>5	ND	2.8	ND	ND
12	ND	>5	ND	8.9	ND	ND
13	ND	>5	ND	9.1	ND	ND
14	ND	>5	ND	1.8	ND	ND
15	ND	>5	ND	2.7	ND	ND
16	ND	>5	ND	9.6	ND	ND
17	ND	>5	ND	1.2	ND	ND
18	ND	>5	ND	5.2	ND	ND
19	ND	>5	ND	0.4	ND	ND
20	ND	>5	ND	7.6	ND	ND
21	ND	>5	ND	0.63	ND	ND
22	ND	>5	ND	9.9	ND	ND
23	ND	>5	ND	>10	ND	ND
24	ND	>5	ND	2.9	ND	ND
25	ND	>5	ND	1.9	ND	ND
26	ND	>5	ND	0.093	0.037	111
27	ND	>5	ND	1.7	ND	ND
28	ND	>5	ND	8.9	ND	ND
29	ND	>5	ND	4.4	ND	ND
30	ND	>5	ND	0.06	0.013	107
31	ND	>5	ND	1.2	ND	ND
32	ND	>5	ND	3	ND	ND
33	ND	>5	ND	>10	ND	ND
34	ND	>5	ND	1.4	ND	ND
35	ND	>5	ND	0.63	ND	ND
36	ND	>5	ND	0.71	ND	ND
37	ND	>5	ND	>10	ND	ND
38	ND	>5	ND	8.5	ND	ND
39	ND	>5	ND	2.1	ND	ND
40	ND	>5	ND	>10	ND	ND
41	ND	>5	ND	0.06	ND	ND
42	ND	>5	ND	1.6	ND	ND
43	ND	>5	ND	>10	ND	ND
44	ND	>5	ND	0.093	ND	ND
45	ND	>5	ND	8.5	ND	ND

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
46	ND	>5	ND	0.005	ND	ND
47	ND	>5	ND	1.2	ND	ND
48	ND	>5	ND	0.02	ND	ND
49	ND	>5	ND	8.8	ND	ND
50	ND	>5	ND	2.2	ND	ND
51	ND	>5	ND	3.3	ND	ND
52	ND	>5	ND	0.029	ND	ND
53	ND	>5	ND	0.44	ND	ND
54	ND	>5	ND	7.3	ND	ND
55	ND	>5	ND	>10	ND	ND
56	ND	>5	ND	0.208	ND	ND
57	ND	>5	ND	0.005	ND	ND
58	ND	>5	ND	2	ND	ND
59	ND	>5	ND	0.65	ND	ND
60	ND	>5	ND	4.2	ND	ND
61	ND	>5	ND	9.5	ND	ND
62	ND	>5	ND	0.42	ND	ND
63	ND	>5	ND	0.57	ND	ND
64	ND	>5	ND	4.8	ND	ND
65	ND	>5	ND	0.69	ND	ND
66	ND	>5	ND	0.78	ND	ND
67	ND	>5	ND	>10	ND	ND
68	ND	>5	ND	9.7	ND	ND
69	ND	>5	ND	0.003	ND	ND
70	ND	>5	ND	3.7	ND	ND
71	ND	>5	ND	0.22	ND	ND
72	ND	>5	ND	1	ND	ND
73	ND	>5	ND	>5	ND	ND
74	ND	>5	ND	0.4	ND	ND
75	ND	>5	ND	0.009	ND	ND
76	ND	>5	ND	0.32	ND	ND
77	ND	>5	ND	2.6	ND	ND
78	ND	>5	ND	>5	ND	ND
79	ND	>5	ND	3.5	ND	ND
80	ND	>5	ND	1.4	ND	ND
81	ND	>5	ND	>5	ND	ND
82	ND	>5	ND	>5	ND	ND
83	ND	>5	ND	0.92	ND	ND
84	ND	>5	ND	0.93	ND	ND
85	ND	>5	ND	2.8	ND	ND
86	ND	>5	ND	0.001	ND	ND
87	ND	>5	ND	0.004	ND	ND
88	ND	>5	ND	0.12	ND	ND
89	ND	>5	ND	0.52	ND	ND
90	ND	>5	ND	3.8	ND	ND
91	ND	>5	ND	0.43	ND	ND
92	ND	>5	ND	1.3	ND	ND
93	ND	>5	ND	0.48	ND	ND
94	ND	>5	ND	3.2	ND	ND

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
95	ND	>5	ND	1.6	ND	ND
96	ND	>5	ND	1.2	ND	ND
97	ND	>5	ND	0.15	ND	ND
98	ND	>5	ND	>10	ND	ND
99	ND	>5	ND	8.4	ND	ND
100	ND	>5	ND	2.4	ND	ND
101	ND	>5	ND	6.1	ND	ND
102	ND	>5	ND	0.38	ND	ND
103	ND	>5	ND	3	ND	ND
104	ND	>5	ND	0.49	ND	ND
105	ND	>5	ND	5.1	ND	ND
106	ND	>5	ND	3	ND	ND
107	ND	>5	ND	2.9	ND	ND
108	ND	>5	ND	0.97	ND	ND
109	ND	>5	ND	>10	ND	ND
110	ND	>5	ND	8.7	ND	ND
111	ND	>5	ND	0.16	ND	ND
112	ND	>5	ND	3.9	ND	ND
113	ND	>5	ND	0.7	ND	ND
114	ND	>5	ND	2.4	ND	ND
115	ND	>5	ND	>10	ND	ND
116	ND	>5	ND	9.5	ND	ND
117	ND	>5	ND	3	ND	ND
118	ND	>5	ND	2	ND	ND
119	ND	>5	ND	3.6	ND	ND
120	ND	>5	ND	>10	ND	ND
121	ND	>5	ND	0.095	ND	ND
122	ND	>5	ND	9.9	ND	ND
123	ND	>5	ND	0.91	ND	ND
124	ND	>5	ND	10	ND	ND
125	ND	>5	ND	0.43	ND	ND
126	ND	ND	ND	ND	ND	ND
127	ND	ND	ND	>5	ND	ND
128	ND	ND	ND	ND	ND	ND
129	ND	ND	ND	ND	ND	ND
130	ND	ND	ND	ND	ND	ND
131	ND	ND	ND	>5	ND	ND
132	ND	ND	ND	ND	ND	ND
133	ND	ND	ND	ND	ND	ND
134	ND	ND	ND	>5	ND	ND
135	ND	ND	ND	ND	ND	ND
136	ND	ND	ND	>5	ND	ND
137	ND	ND	ND	>5	ND	ND
138	ND	ND	ND	>5	ND	ND
139	ND	ND	ND	>5	ND	ND
140	ND	ND	ND	>5	ND	ND
141	ND	ND	ND	>5	ND	ND
142	ND	ND	ND	>5	ND	ND
143	ND	ND	ND	>5	ND	ND

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
144	ND	ND	ND	>5	ND	ND
145	ND	ND	ND	>5	ND	ND
146	ND	ND	ND	>5	ND	ND
147	ND	ND	ND	>5	ND	ND
148	ND	ND	ND	ND	ND	ND
149	ND	ND	ND	>5	ND	ND
150	ND	ND	ND	>5	ND	ND
151	ND	ND	ND	>5	ND	ND
152	ND	ND	ND	>5	ND	ND
153	ND	ND	ND	>5	ND	ND
154	ND	ND	ND	>5	ND	ND
155	ND	ND	ND	>5	ND	ND
156	ND	ND	ND	>5	ND	ND
157	ND	ND	ND	>5	ND	ND
158	ND	ND	ND	>5	ND	ND
159	ND	ND	ND	>5	ND	ND
160	ND	ND	ND	0.66	0.45	ND
161	ND	ND	ND	ND	ND	ND
162	ND	ND	ND	ND	ND	ND
163	ND	ND	ND	ND	ND	ND
164	ND	ND	ND	ND	ND	ND
165	ND	ND	ND	1.1	0.7	ND
166	ND	ND	ND	0.61	0.73	ND
167	ND	ND	ND	ND	ND	ND
168	ND	ND	ND	ND	ND	ND
169	ND	ND	ND	ND	ND	ND
170	ND	ND	ND	ND	ND	ND
171	ND	ND	ND	0.53	1.2	ND
172	ND	ND	ND	ND	ND	ND
173	ND	ND	ND	2	0.92	ND
174	ND	ND	ND	0.61	0.84	ND
175	ND	ND	ND	ND	ND	ND
176	ND	ND	ND	>10	>10	ND
177	ND	ND	ND	ND	ND	ND
178	ND	ND	ND	ND	ND	ND
179	ND	ND	ND	>10	>10	ND
180	ND	ND	ND	0.17	0.12	ND
181	ND	ND	ND	1	0.57	ND
182	ND	ND	ND	ND	ND	ND
183	ND	ND	ND	ND	ND	ND
184	ND	ND	ND	0.74	0.69	ND
185	ND	ND	ND	ND	ND	ND
186	ND	ND	ND	ND	ND	ND
187	ND	ND	ND	ND	ND	ND
188	ND	ND	ND	ND	ND	ND
189	ND	ND	ND	ND	ND	ND
190	ND	ND	ND	0.34	0.34	ND
191	ND	ND	ND	ND	ND	ND
192	ND	ND	ND	ND	ND	ND

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
193	ND	ND	ND	0.27	0.25	ND
194	ND	ND	ND	0.037	0.035	ND
195	ND	ND	ND	0.026	0.026	ND
196	ND	ND	ND	0.043	0.049	ND
197	ND	ND	ND	0.021	0.02	ND
198	ND	ND	ND	1	1.3	ND
199	ND	ND	ND	0.82	2.4	ND
200	ND	ND	ND	0.53	0.34	ND
201	ND	ND	ND	ND	ND	ND
202	ND	ND	ND	0.058	0.053	ND
203	ND	ND	ND	0.2	0.18	ND
204	ND	ND	ND	ND	ND	ND
205	ND	ND	ND	0.072	0.071	ND
206	ND	ND	ND	0.042	0.048	ND
207	ND	ND	ND	0.048	0.05	ND
208	ND	ND	ND	ND	ND	ND
209	ND	ND	ND	ND	ND	ND
210	ND	ND	ND	ND	ND	ND
211	ND	ND	ND	1.3	1	ND
212	ND	ND	ND	>10	>10	ND
213	ND	ND	ND	0.36	0.36	ND
214	ND	ND	ND	ND	ND	ND
215	ND	ND	ND	0.17	0.3	ND
216	ND	ND	ND	0.45	>10	ND
217	ND	ND	ND	ND	ND	ND
218	ND	ND	ND	ND	ND	ND
219	ND	ND	ND	ND	ND	ND
220	ND	ND	ND	0.54	0.72	ND
221	ND	ND	ND	0.029	0.029	ND
222	ND	ND	ND	>10	>10	ND
223	ND	ND	ND	0.54	1.4	ND
224	ND	ND	ND	ND	ND	ND
225	ND	ND	ND	0.32	0.19	ND
226	ND	ND	ND	ND	ND	ND
227	ND	ND	ND	ND	ND	ND
228	ND	ND	ND	ND	ND	ND
229	ND	ND	ND	ND	ND	ND
230	ND	ND	ND	0.81	2.5	ND
231	ND	ND	ND	0.067	0.074	ND
232	ND	ND	ND	ND	ND	ND
233	ND	ND	ND	0.53	0.88	ND
234	ND	ND	ND	0.95	0.61	ND
235	ND	ND	ND	1.6	3.8	ND
236	ND	ND	ND	ND	ND	ND
237	ND	ND	ND	4.4	1	ND
238	ND	ND	ND	0.65	0.55	ND
239	ND	ND	ND	ND	ND	ND
240	ND	ND	ND	ND	ND	ND
241	ND	ND	ND	0.28	0.23	ND

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
242	ND	ND	ND	4.4	5	ND
243	ND	ND	ND	ND	ND	ND
244	ND	ND	ND	0.67	3	ND
245	ND	ND	ND	ND	ND	ND
246	ND	ND	ND	ND	ND	ND
247	ND	ND	ND	ND	ND	ND
248	ND	ND	ND	1.6	1.7	ND
249	ND	ND	ND	ND	ND	ND
250	ND	ND	ND	ND	ND	ND
251	>5	>5	>5	0.004	ND	92
252	>5	>5	>5	0.94	0.63	ND
253	>5	>5	>5	0.063	0.05	99
254	>5	>5	>5	0.043	ND	103
255	>5	>5	>5	0.074	ND	95
256	>5	>5	>5	0.12	ND	92
257	>5	>5	>5	0.11	ND	88
258	>5	>5	>5	0.1	ND	ND
259	>5	>5	>5	0.15	0.087	101
260	>5	>5	>5	0.014	ND	ND
261	>5	>5	>5	0.59	ND	ND
262	>5	>5	>5	0.79	ND	ND
263	ND	>5	>5	0.004	0.003	97
264	ND	>5	>5	0.18	0.1	139
265	>5	>5	>5	0.005	0.005	90
266	>5	>5	>5	0.0005	0.0004	ND
267	>5	>5	>5	0.15	0.15	ND
268	>5	>5	>5	0.13	0.12	ND
269	>5	>5	>5	0.79	ND	ND
270	>5	>5	>5	>10	>10	ND
271	>5	>5	>5	5.4	2.9	ND
272	>5	>5	>5	0.117	0.21	ND
273	>5	ND	>5	7	6.5	ND
274	>5	ND	>5	4.8	1.5	ND
275	>5	>5	>5	0.042	0.019	103
276	ND	>5	>5	1.1	ND	ND
277	>5	>5	>5	0.89	1.6	ND
278	>5	>5	>5	0.028	0.012	ND
279	>5	>5	>5	0.13	0.068	ND
280	>5	>5	>5	ND	ND	90
281	>5	>5	>5	>10	>10	ND
282	>5	>5	>5	0.38	0.313	ND
283	>5	>5	>5	>10	>10	ND
284	>5	>5	>5	>10	>10	ND
285	ND	>5	>5	ND	ND	ND
286	ND	>5	>5	ND	ND	ND
287	ND	>5	>5	ND	ND	ND
288	ND	>5	>5	ND	ND	ND
289	ND	>5	>5	ND	ND	ND
290	>5	>5	>5	0.038	0.019	101

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
291	ND	ND	ND	ND	ND	ND
292	>5	>5	>5	0.11	0.084	ND
293	>5	>5	>5	0.19	0.17	ND
294	>5	>5	>5	0.051	0.05	101
295	>5	>5	>5	0.0047	0.0045	101
296	>5	>5	>5	0.048	0.043	98
297	>5	>5	>5	0.032	0.045	103
298	>5	>5	>5	0.03	0.044	103
299	>5	>5	>5	0.14	0.16	103
300	>5	>5	>5	0.013	0.013	90
301	>5	>5	>5	0.032	0.032	101
302	>5	>5	>5	0.006	0.006	107
303	>5	>5	>5	0.004	0.006	93
304	>5	>5	>5	0.15	0.18	85
305	ND	>5	>5	ND	ND	ND
306	>5	>5	>5	0.044	0.035	ND
307	ND	>5	>5	ND	ND	ND
308	>5	>5	>5	0.36	0.3	ND
309	ND	>5	>5	ND	ND	ND
310	>5	>5	>5	0.034	0.034	ND
311	>5	>5	>5	0.00047	0.00034	95
312	>5	>5	>5	0.032	0.024	ND
313	>5	>5	>5	0.035	0.02	ND
314	>5	>5	>5	0.13	0.1	110
315	ND	ND	ND	0.8	2	ND
316	ND	ND	ND	ND	ND	ND
317	ND	ND	ND	0.01	0.011	ND
318	ND	ND	ND	ND	ND	ND
319	ND	ND	ND	ND	ND	ND
320	ND	ND	ND	ND	ND	ND
321	ND	ND	ND	ND	ND	ND
322	ND	>5	ND	ND	ND	ND
323	>5	ND	>5	0.026	0.026	ND
324	>5	>5	>5	0.39	0.69	ND
325	>5	>5	>5	0.006	0.004	ND
326	ND	>5	>5	ND	ND	ND
327	>5	>5	>5	0.11	0.06	101
328	ND	>5	>5	ND	ND	ND
329	>5	>5	>5	0.02	0.016	ND
330	>5	>5	>5	0.44	0.26	99
331	ND	>5	>5	ND	ND	ND
332	>5	>5	>5	0.61	0.53	ND
333	ND	>5	>5	ND	ND	ND
334	ND	>5	>5	ND	ND	ND
335	>5	>5	>5	0.11	0.098	ND
336	>5	>5	>5	0.22	0.205	ND
337	>5	ND	>5	0.096	0.108	ND
338	>5	>5	>5	0.91	1.2	ND
339	>5	>5	>5	0.034	0.031	ND

Compound	hNPY1	hNPY2	hNPY4	hNPY5	rNPY5	rNPY5
340	>5	>5	>5	0.227	0.25	ND
341	>5	>5	>5	0.33	0.29	ND
342	>5	>5	>5	0.276	0.37	105
343	>5	>5	>5	0.11	0.045	ND
344	>5	>5	>5	2.7	1.7	ND
345	>5	>5	>5	2.9	3.3	93
346	>5	>5	>5	0.081	0.063	105
347	>5	>5	>5	0.143	0.13	ND
348	>5	>5	>5	1.2	>10	ND
349	>5	>5	>5	0.138	0.165	100
350	>5	>5	>5	2.3	1.4	ND
351	>5	>5	>5	0.58	0.979	ND
352	>5	>5	>5	0.053	0.0628	90
353	>5	>5	>5	0.135	0.187	ND
354	>5	>5	>5	0.143	0.136	98
355	>5	>5	>5	0.2	0.19	ND
356	>5	>5	>5	0.259	0.271	105
357	>5	>5	>5	0.239	0.229	112
358	>5	>5	>5	0.73	0.443	ND
359	>5	>5	>5	1.3	1.2	104
360	>5	>5	>5	0.055	0.0562	ND
361	>5	>5	>5	0.41	0.539	ND
362	>5	ND	>5	0.2	0.115	ND

Compounds 330-362, each tested according to one or more assays set forth in this Example are known compounds. The name of each known compound and it source is set forth in Table 4 immediately below.

TABLE 4

Compound	NAME	Reference
330	N-(2,6-Dibromo-4-ethyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
331	N-(2-Amino-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
332	N-(2,4-Difluoro-benzyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
333	5-Chloro-2-{2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino}-benzoic acid methyl ester	EP-628555-A1
334	5-Amino-2-{2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino}-benzamide	EP-628555-A1
335	N-(2-Amino-4-benzenesulfonyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
336	N-(4-Diethylamino-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
337	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-phenylamino-phenyl)-acetamide	EP-628555-A1
338	N-(3-Dimethylamino-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1

Compound	NAME	Reference
339	N-(2-Amino-4-propylsulfanyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide; compound with GENERIC INORGANIC NEUTRAL COMPONENT	EP-628555-A1
340	N-(7-Hydroxy-naphthalen-1-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
341	N-(4-Chloro-3-nitro-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
342	N-(4-Bromo-3-chloro-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
343	N-(7-Butoxy-naphthalen-2-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
344	N-(1H-Indazol-6-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
345	N-(4-Hydroxy-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
346	N-(4-Ethoxy-naphthalen-1-yl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
347	N-(4-Ethoxy-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
348	N-(2-Chloro-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
349	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-phenylazo-phenyl)-acetamide	EP-628555-A1
350	4-(2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino)-benzamide	EP-628555-A1
351	N-(4-Acetylamino-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
352	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-phenoxy-phenyl)-acetamide	EP-628555-A1
353	N-(4-Dimethylamino-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
354	N-(4-Acetyl-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
355	N-(4-Nitro-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
356	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-(4-trifluoromethyl-phenyl)-acetamide	EP-628555-A1
357	N-(3-Chloro-4-nitro-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
358	N-(4-Chloro-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
359	2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-N-p-tolyl-acetamide	EP-628555-A1
360	4-[2-[4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetylamino]-benzoic acid methyl ester	EP-628555-A1
361	N-(4-Methoxy-phenyl)-2-[4-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-piperidin-1-yl]-acetamide	EP-628555-A1
362	N-(4-Cyclohexyl-phenyl)-2-morpholin-4-yl-acetamide	G & J JS 380

EXAMPLE 6

This example describes the preparation of a tablet that includes composition 1 as prepared in Example 2.

Formulation of a coated tablet according to the invention:

Compound 251 of Example 3	583.0 mg
Microcrystalline cellulose	55.0 mg
Corn starch	72.0 mg
Poly(1-vinyl-2-pyrrolidone)	30.0 mg
Highly dispersed silica	5.0 mg
Magnesium stearate	5.0 mg
Total	750.0 mg

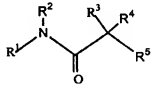
The tablet coating contains:

Poly(O-hydroxypropyl O-methyl)-cellulose 15 cp	6.0 mg
Macrogol 4000 rec. INN	2.0 mg
(polyethylene glycol DAB)	2.0 mg
Titanium(IV) oxide	10.0 mg

While the present invention has been described by means of specific embodiments, it will be understood that modifications may be made without departing from the spirit of the invention. The scope of the invention is not to be considered as limited by the description of the invention set forth in the specification and examples.

What we claim is:

1. A method for treating mammalian disorders mediated by the NPY Y5 receptor comprising administering to the mammal a therapeutically effective amount of at least one compound having the formula:



or pharmaceutically acceptable salts thereof wherein R_1-R_5 are each individually selected from the group of substituents including hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, and cyano.

2. The method according to claim 1 wherein R^1 is cyclohexyl; benzoyl; phenyl; phenyl substituted at least once with a lower alkyl that is in turn substituted at least once with a substituent selected from cycloalkyl, alkoxy, furan, oxo, phenyl, diisopropylamine, alkoxy, or mixtures thereof, lower alkyl, alkyl substituted at least once by oxo, phenyl, or by mixtures thereof, phenyl substituted alkene, carboxamide, carboalkoxy, methyl substituted carbophenoxy, phenyldiazo, halogen, nitro, trifluoroalkyl, amino, phenyl substituted amino, lower alkyl substituted amino, aminoacyl, sulfonylphenyl, hydroxy, alkoxy, fluoro substituted phenyl, oxazole, phenoxy, thioalkoxy, and mixtures thereof; hydroxy or alkoxy substituted naphthyl; 1H-indazole; fluorenone; fluorene; and phenyl.

3. The method according to claim 1 wherein R^2 is selected from the group hydrogen and lower alkyl.

4. The method according to claim 1 wherein R^3 and R^4 are each individually selected from the group hydrogen, lower alkyl, and phenyl.

5. The method according to claim 1 wherein R^3 and R^4 are each individually selected from hydrogen or methyl.

6. The method according to claim 1 wherein R^5 is pyrrolidine; pyrrolidine substituted at least once by amino, acylamino, trifluoroacylamino, hydroxyl, carboxyl, carbobenzyloxyamino, carbomethoxyamino, carbotertbutoxyamino, alkyl substituted carbotertbutoxyamino, pyridine, lower alkyl, alkene, carboxamide, hydroxymethyl, aminoalkyl, pyrolidinemethyl, alkoxy methyl, carboxylmethyl, hydroxymethyl substituted at least once by phenyl and mixtures thereof; morpholine; piperazine substituted at least once with benzyl, phenyl, halogen substituted phenyl, and mixtures thereof; unsubstituted piperidine; substituted piperidine; piperidine substituted at least once by 2-oxo-2,3-dihydrobenzimidaz-1-ol, unsubstituted lower alkyl, lower alkyl substituted at least once by aminoethylamino, iodide, =O, piperidine, hydroxymethyl substituted piperdine, acylamino, hydroxyl, phenyl, and mixtures thereof, cyano, halogen, cyanomethylphenyl, piperidine, pyrolidine, carboxyl, phenyl, phenyl substituted at least once by trifluoromethyl, lower alkyl, halogen, and mixtures thereof, 4-oxo-1-phenyl-1,3,8-triazaspiro[4.5dec-8-yl], hydroxyl, alkoxy, carboxyl amide having the formula $CONR^8R^9$ wherein R^8 and R^9 are each individually hydrogen or lower alkyl, or R^8 and R^9 are united with a nitrogen atom to form a piperidine substituent, amino alkyl having the formula $NR^{10}R^{11}$ where R^{10} and R^{11} are each individually selected from lower alkyl, cycloalkyl and phenyl, a ketone having the formula -COR^{12} where R^{12} is phenyl substituted by halogen or alkoxy or mixtures thereof; 3,6-

dihydro-2H-pyridin-1-yl; halogen substituted phenyl substituted 3,6-dihydro-2H-pyridin-1-yl; 1,3,3-trimethyl-6-aza-bicyclo[3.2.1]octyl-6-yl; 2-aza-bicyclo[2.2.1]hept-6-yl; an amine having the formula NR^6R^7 where R^6 and R^7 are the each individually selected from hydrogen, unsubstituted and substituted alkyl having from 1 to 10 carbon atoms, cycloalkyl, alkene, carboxy substituted alkene, lower alkyl substituted at least once by cyano, alkyne, cycloalkyl, hydroxyl, 2-hydroxyethoxy, pyridine, piperidine, pyrrolidine, piperazine, morpholine, methylpiperazine, 1-Methylpyrrol, phenyl, phenyl substituted at least once by alkoxy, halogen, carboxyl, phenoxy, hydroxy, nitro, iodine, and mixtures thereof, imidazole, 5-nitropyridylamino, furan, benzo[1,3]dioxol-5-yl, indole, alkoxy substituted indole, diethylamino, alkoxy, carboxy, trifluoromethyl, lower alkyl, hydroxymethyl, and mixtures thereof, benzyl, phenyl, benzo[1,2,5]thiadiazol, pyridine, 1,2,4-triazole, and 3-oxo-cyclohex-1-en.

7. The method according to claim 1 wherein the pharmaceutical result is the treatment of mammals with disorders selected from obesity and eating disorders.

8. The method according to claim 7 wherein the mammal is a human and the eating disorder is selected from the group consisting of bulimia and obesity.

9. The method according to claim 1 wherein the pharmaceutical result is the treatment of obesity related disorders.

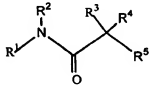
10. The method according to claim 1 wherein the mammal is a human.

11. The method according to claim 1 wherein the therapeutically effective amount ranges from about 0.001 to about 100 mg/kg weight of the mammal.

12. The method according to claim 1 wherein the composition is administered orally in the form of a solution.

13. The method according to claim 1 wherein the composition is administered orally in the form of a tablet.

14. A composition of matter having the formula:



or pharmaceutically acceptable salts thereof wherein R_1-R_5 are each individually selected from the group of substituents including hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, and cyano, and wherein the compound is not a compound selected from compounds 330-362 of Table 4.

15. The composition according to claim 14 wherein R^1 is cyclohexyl; benzoyl; phenyl; phenyl substituted at least once with a lower alkyl that is in turn substituted at least once with a substituent selected from cycloalkyl, alkoxy, furan, oxo, phenyl, diisopropylamine, alkoxy, or mixtures thereof, lower alkyl, alkyl substituted at least once by oxo, phenyl, or by mixtures thereof, phenyl substituted alkene, carboxamide, carboalkoxy, methyl substituted carbophenoxy, phenyldiazo, halogen, nitro, trifluoroalkyl, amino, phenyl substituted amino, lower alkyl substituted amino, aminoacyl, sulfonylphenyl, hydroxy, alkoxy, fluoro substituted phenyl, oxazole, phenoxy, thioalkoxy, and mixtures thereof; hydroxy or alkoxy substituted naphthyl; 1H-indazole; fluorenone; fluorene; and phenyl.

16. The composition according to claim 14 wherein R^2 is hydrogen or lower alkyl.

17. The method according to claim 14 wherein R^3 and R^4 are each individually selected from the group hydrogen, lower alkyl, and phenyl.

18. The method according to claim 14 wherein R^3 and R^4 are each individually selected from hydrogen or methyl.

19. The composition according to claim 14 wherein R^5 is pyrrolidine; pyrrolidine substituted at least once by amino, acylamino, trifluoroacylamino, hydroxyl, carboxyl, carbobenzyloxyamino, carbomethoxyamino, carbotertbutoxyamino, alkyl substituted carbotertbutoxyamino, pyridine, lower alkyl, alkene, carboxamide, hydroxymethyl, aminoalkyl, pyrolidinemethyl, alkoxy methyl, carboxylmethyl, hydroxymethyl substituted at least once by phenyl and mixtures thereof; morpholine; piperazine substituted at least once with benzyl, phenyl, halogen substituted phenyl, and mixtures thereof; unsubstituted piperidine; substituted piperidine; piperidine substituted at least once by 2-oxo-2,3-dihydrobenzimidaz-1-ol, unsubstituted lower alkyl, lower alkyl substituted at least once by aminoethylamino, iodide, =O, piperidine, hydroxymethyl substituted piperdine, acylamino, hydroxyl, phenyl, and mixtures thereof, cyano, halogen, cyanomethylphenyl, piperidine, pyrolidine, carboxyl, phenyl, phenyl substituted at least once by trifluoromethyl, lower alkyl, halogen, and mixtures thereof, 4-oxo-1-phenyl-1,3,8-triazaspiro[4.5dec-8-yl], hydroxyl, alkoxy, carboxyl amide having the formula $CONR^8R^9$ wherein R^8 and R^9 are each individually hydrogen or lower alkyl, or R^8 and R^9 are united with a nitrogen atom to form a piperidine substituent, amino alkyl having the formula $NR^{10}R^{11}$ where R^{10} and R^{11} are each individually selected from lower alkyl, cycloalkyl and phenyl, a ketone having the formula $-COR^{12}$ where R^{12} is phenyl substituted by halogen or alkoxy or mixtures thereof; 3,6-dihydro-2H-pyridin-1-yl; halogen substituted phenyl substituted 3,6-dihydro-2H-pyridin-1-yl; 1,3,3-trimethyl-6-aza-bicyclo[3.2.1]octyl-6-yl; 2-aza-bicyclo[2.2.1]hept-6-yl; an amine

having the formula NR^6R^7 where R^6 and R^7 are the each individually selected from hydrogen, unsubstituted and substituted alkyl having from 1 to 10 carbon atoms, cycloalkyl, alkene, carboxy substituted alkene, lower alkyl substituted at least once by cyano, alkyne, cycloalkyl, hydroxyl, 2-hydroxyethoxy, pyridine, piperidine, pyrrolidine, piperazine, morpholine, methylpiperazine, 1-Methylpyrrol, phenyl, phenyl substituted at least once by alkoxy, halogen, carboxyl, phenoxy, hydroxy, nitro, iodine, and mixtures thereof, imidazole, 5-nitropyridylamino, furan, benzo[1,3]dioxol-5-yl, indole, alkoxy substituted indole, diethylamino, alkoxy, carboxy, trifluoromethyl, lower alkyl, hydroxymethyl, and mixtures thereof, benzyl, phenyl, benzo[1,2,5]thiadiazol, pyridine, 1,2,4-triazole, and 3-oxo-cyclohex-1-en.

20. A pharmaceutical dosage form comprising the composition of claim 14 and at least one pharmaceutical additive.

21. The pharmaceutical dosage form of claim 20 wherein the pharmaceutical dosage form is administered by a method selected from oral administration, dermal administration, injection, implant, inhalation, intravenously, and by suppository.

INTERNATIONAL SEARCH REPORT

Inter ional Application No
PCT/US 98/02121

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D401/04 C07C237/04 C07D407/14 C07D401/14 A61K31/445
C07D207/14 C07D211/58 C07D213/57 C07D213/26 C07D407/06
C07D295/073

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D C07C A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	S. BUDAVARI ET AL.: "The Merck Index" 1996 , MERCK RESEARCH LABORATORIES , WHITEHOUSE STATION, NJ XP002069058 * 47. Acetanilide * see page 9 - page 10 --- -/--	14-16

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
10 July 1998	03. 07. 98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Herz, C

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X	DE 575 858 C (I.G. FARBENINDUSTRIE AKT.-GES.) 13 April 1933 see page 3 ---	14-16
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A	WO 92 06079 A (PFIZER INC.) 16 April 1992 see claims 1-40 ---	14-21
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A	EP 0 747 356 A (BRISTOL-MYERS SQUIBB COMPANY) 11 December 1996 see claims 1-10 ---	14-21
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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte. ..onal Application No
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